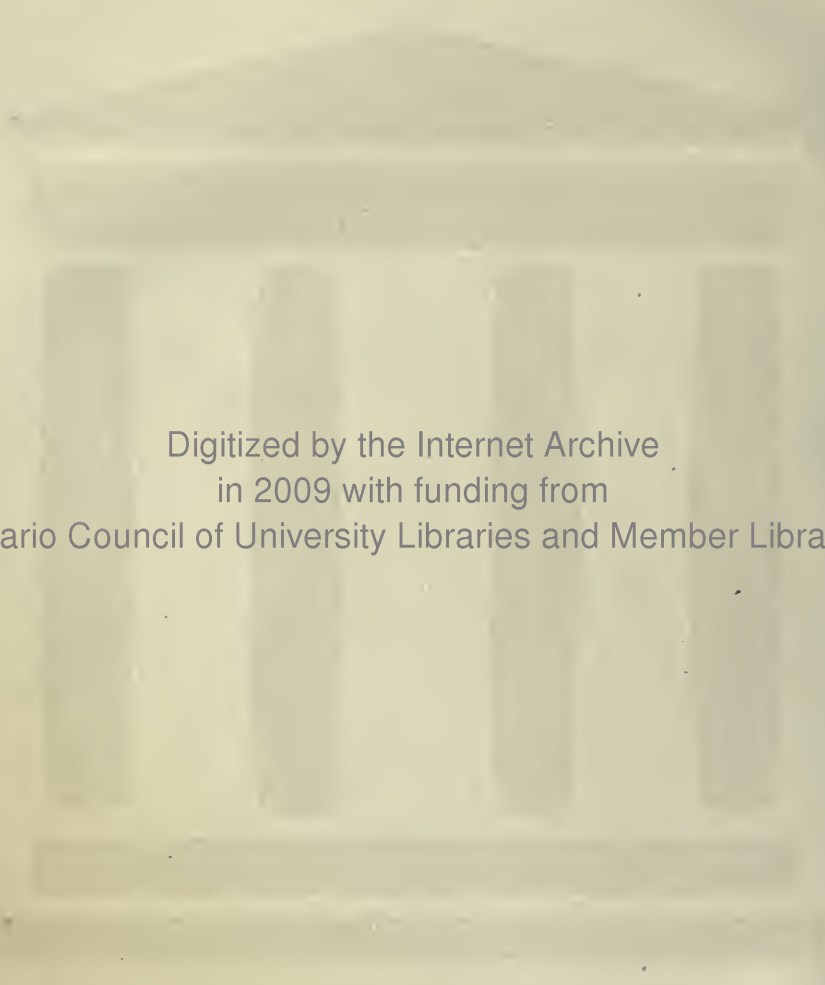


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1

THE JOURNAL OF UROLOGY BECOMES THE OFFICIAL ORGAN OF THE AMERICAN UROLOGICAL ASSOCIATION

At the last annual meeting of the American Urological Association a committee was appointed by the president which was empowered to establish an official journal of the association. This committee decided that the present JOURNAL OF UROLOGY offered the best medium of expression for urological literature. Arrangements have been completed whereby the JOURNAL has become the property of the association and subject to its control. It will continue to be published by the Williams & Wilkins Company of Baltimore and under the editorship of Dr. Hugh Young. Coöperating with him will be an executive editorial committee consisting of Leo Buerger, H. A. Fowler, W. C. Quinby, Hugh H. Young and W. F. Braasch. There are also a number of collaborators from all sections of the country, including the former associate editors, who will be relied upon for active editorial support.

Commencing with the next issue, the JOURNAL OF UROLOGY will be published as the official organ of the American Urological Association. According to the action of the association at its last meeting, every member of the association will become a subscriber to the JOURNAL, the subscription fee being included in the annual dues.

It is the intention of the editorial board to continue the JOURNAL as a thoroughly representative expression of American urology. Particularly do they wish to make it of live clinical interest to the urologist. In order to bring this about, it will be necessary to have the active support of the members of the association. It will be the JOURNAL's policy to publish papers of merit on all phases of urology. It will publish papers read at the annual meeting of the American Urological Association as well as of its branches. It is hoped that in the near future new

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FOREWORD

departments may be added that should increase the value of the JOURNAL. Among these is a section devoted to new instruments, methods of surgical technique, case reports, etc. Contributions of this character are particularly solicited from every member.

The JOURNAL will be published monthly, providing that there is sufficient material submitted.

213 Ball Building,
Cleveland.

H. L. SANFORD,
Secretary.

The above announcement from the secretary of the American Urological Association states succinctly the conditions which led the editorial board under which the JOURNAL OF UROLOGY has flourished for four years, to turn over their responsibility to the American Urological Association. This has been done at a time when considerable increase in subscribers, advertising matter and support from urologists both in America and abroad insured a brilliant future, because we felt that it would greatly strengthen the JOURNAL OF UROLOGY to have behind it the great influence of the American Urological Association.

The original editorial board remains, now consolidated with additions from the American Urological Association. An executive editorial committee, of which Dr. Wm. F. Braasch is chairman, will be responsible to the association for the conduct of the JOURNAL.

The editor takes this opportunity to express his gratitude to his co-editors for their splendid assistance in the past, and to bespeak for the JOURNAL the continued support of those individual contributors, clinics and laboratories which have made the JOURNAL OF UROLOGY real archives of the science and art of urology, worthy of the best in American medicine. With the active interest and assistance of the great membership of the American Urological Association to guide, counsel and contribute to its success, we feel very happy in this assurance of prosperity and perpetuity for the JOURNAL OF UROLOGY.

HUGH H. YOUNG.

TRAUMA AS A FACTOR IN THE ETIOLOGY OF HYDRONEPHROSIS (PYELECTASIS)

FREDERICK C. HERRICK

Cleveland, Ohio

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I. TERMINOLOGY

In the voluminous literature on the subject of hydronephrosis, it is evident that the one constant factor present is dilatation of the renal pelvis as a whole or in part. The term applied describes the contents of the sac rather than the pathological condition. Those interested have fallen into the habit of calling the condition hydronephrosis following some early writers, notably Rayer (1), who considered a water-like fluid to be the contents. In retaining this term, the fact that pus, blood or no retained fluid may be present instead of water has been disregarded. In recent studies of the subject, the fact should be clearly recognized that ectasia is the uniform result of many etiological factors, and that, while analyzing these factors, their one constant result should be a well defined entity. Old terms, therefore, do not define the condition, and follow neither anatomical nor physiological indications, but seem to rely upon the one fixed idea of a water contents, thus, hydrops renis (Martineau 1785, (2)), hydrourenal distension (Johnson 1816 (3)), hydronephrosis (Rayer, 1841). Expression of the idea of dilatation in the term was first made by Morris (4) in 1894, by the use of nephrectasis, meaning a dilatation of the entire kidney. In many cases, especially the early ones, in which we are most interested, the pelvic dilatation is the only departure from the normal, barring lesser microscopical changes in the kidney from back pressure. Pereshivkin (5) (1913) has suggested the term pyelectasis. The writer has used this term for several years independently.

Many writers, therefore, making special study of the subject have suggested different terms. This is the best evidence that no term has conveyed a satisfactory conception of the pathological or clinical condition. Why not by a simple analysis apply a name fitting the condition accurately? Thus pyelum, pelvis; *εκ*, out; *τεινειν*, to distend, with the proper termination, *pyelectasis*. Words influence our conception of a condition and lead us to inaccuracies. We recognize bronchiectasis, telangiectasis, gastrectasis and pyelectasis. The fitting term pyonephrosis is still retained, for in this condition the entire kidney is involved in the infective process. Pyo-pyelectasis expresses

dilatation with pus as a contents, and together with hemo-pyelectasis and uro-pyelectasis accurately describes well recognized clinical conditions. All these terms are easy of pronunciation.

II. MECHANICAL OBSTRUCTION

In the acquired form of pyelectasis following trauma, to which this paper is confined, the next characteristic seems to be a physiological one, *i.e.*, a motor insufficiency. The renal pelvis and ureter according to Satani (6), and others possess an intrinsic power of peristaltic contraction.

The amplitude and rate of the spontaneous contractions vary in different parts of the ureter. The contractions of the middle part are large and slow, those of the kidney portion are lower and faster, while at the bladder end the contractions are very small in size and slow in rate. These differences so far as size is concerned are correlated with the different thicknesses of the circular muscular coat which has its largest development in the middle section. (Satani.)

Mechanical resistance to this expulsive effort may be partial or complete with consequent back pressure and beginning dilatation. Some form of obstruction is essential whether from swollen mucosa, the products of an inflammatory process, a ureteral kink or some other of the recognized active factors. No matter how atonic or atrophied the renal pelvic and ureteral musculature may be their distension does not seem possible without mechanical obstruction as the first stage. Compare hollow muscular organs in other parts of the body which are subject to inflammatory processes. Tuberculosis of the bladder is characterized by a small bladder.

Cholecystitis, when not influenced by bile duct obstruction, tends to make a thick-walled smaller-cavities viscus. In the stomach condition known as linitis plastica, without pyloric obstruction, we find a small leather bottle type of viscus. In non-syphilitic arteritis the muscle is intact and the vessels not dilated. A chronic inflammatory process tends to lessen a physiological cavity which has an open outlet.

Neither from the neurological viewpoint does dilatation seem possible without mechanical obstruction. If each successive peristaltic wave forms a cavity of the section of ureter involved this pocket of urine, grasped and carried toward the bladder might be under sufficient tension to result in stretching of the ureteral muscle, if this muscle is injured by infection. Under these conditions a muscle would be stretched by its own effort at contraction which is recognized by physiologists as a possibility in the heart. A further study of the nervous control of the ureter may elucidate this point. The irregularity of the musculature and contractions of the ureter (as above quoted) might help this claim and a further study of the nervous control of the ureter may show periodic or localized spasmodic contractions. Such contractions would, however, be mechanical in effect and dilatations following them would be mechanical and not inflammatory.

From the clinical standpoint, motor insufficiency working against an obstruction for which it is unable to compensate, results in the retention with the ectasia. Dilatation of the pelvis tends to conserve the renal secreting surface by lessening back pressure. In partial and complete ureteral obstruction this process does not go on indefinitely, but is limited by secondary changes within the secreting mechanism. Ghoreyeb (7) studied the effect of pelvic dilatation on the blood volume passing through the kidney and consequently on the volume of urine secreted. At the end of one week there was in his rabbits an impediment to the renal circulation due to cicatricial changes within the organ which tend to maintain the tubules dilated and in a position of encroachment on the space normally allotted to the blood vessels. Secretion is limited when pressure against it has passed of the average 70 mm. of mercury in the dog (Cushny (8)).

III. CLINICAL STATUS OF TRAUMA AS A FACTOR

The old clinical practice of recognizing only such pelves as hydronephrotic which showed a very large dilatation has to urologists fortunately long passed, but not so to many general

surgeons or internists. The lesser dilatations may be actually indeterminable from a volumetric standpoint and may be recognized from the physiological criterion of failing to empty themselves, a motor insufficiency, an intermittent pyelectasis in the earliest stage. Those dilatations large or small resulting from mechanical factors due to trauma, so-called subcutaneous, sub-parietal, blunt, or muscular violence have been of special interest to the writer. These form two groups:

1. Those cases in which the demonstrable tumor develops within a few days or weeks after the injury comprise a group for long erroneously considered as composed of true renal pelvic dilatation. Wagner (9), Küster (10), Delbet (11) at first thought them genuine. Morris (12), Monod (13), and Legueu (14), showed the contrary and recently Watson and Cunningham, Keyes and others have expressed the same opinion.

Monod (1892) recognized but three and Wagner (1911) but ten genuine cases of rapidly forming (within a month) genuine post-traumatic hydronephroses. In the others rupture of the renal pelvis or ureter resulted in rapidly accumulating collections of blood and urine held within the renal fascia, which fascia fusing with the kidney formed to all appearances part of the true pelvis greatly dilated. This led to Wagner's and Simon's erroneous conclusion that feeling the renal calyces within the sac was proof of the sac's being entirely of pelvic origin.

2. Those cases in which, after a variable period of disability following the injury go about their usual activities but begin to notice gradually increasing more or less marked symptoms of pain, increased frequency, possibly cloudy urine or occasional hematuria.

In cases of the first group the history of trauma and succeeding illness are unmistakable; in those of the second the history of trauma is easily overlooked and may have occurred one or many years before consultation. These cases present diagnostic pitfalls for the unwary clinician. Braasch (15) reports 35 per cent as having been operated on a wrong diagnosis. Fowler (16) 45 per cent. Of the author's cases of early pyelectasis 7 of 18, or 38 per cent, had been operated on a wrong diagnosis.

Regarding the clinical association of trauma and pyelectasis, Delbet, in 321 cases of renal trauma found pyelectasis developed later in 6.3 per cent. Suter (17) in 522 blunt renal traumas found it in 8.2 per cent. Moser (18) in 103 found it in 6.8 per cent—an average of 7.1 per cent for 946 cases. These figures, however, were collected before a proper distinction was drawn between traumatic pseudo and genuine hydronephrosis, but also before the lesser results of traumatic angulation, ptosis, temporary obstruction, etc. had been appreciated. Tuffier found 12 pyelectases in 40 operated moveable kidneys. Watson and Cunningham found 83 cases in the literature of ureteral kinks from mobility. Kelley found in a group of 64 movable kidneys that 9 showed “increasing pelvic capacity” and in 1914 recognized that abnormal “mobility of the kidney is undoubtedly the commonest single cause” of pyelectasis (p. 530, vi). The latter statement, however, is open to question today in the light of work, experimental and clinical, on inflammatory ureteral strictures. Such strictures when associated with some of the factors to be later mentioned may be especially potent as causes.

Our present knowledge of the subject of pyelectasis, renders any classification of the etiological factors as tentative, and chiefly for purposes of study. Placing all such factors under the three heads of obstructive, inflammatory and neurological does not seem sufficiently analytic. For the present, and in order to find the relation of trauma to other factors, I have made the following classification.

IV. ETIOLOGY OF PYELECTASIS (HYDRONEPHROSIS)

I. *Congenital*

Condition present at birth.

II. *Acquired*

1. *Predisposing factors*

Anatomical in character; partly congenital; quiescent; becoming active because of some acquired condition. Their degree and relation to active factors determine their potency.

a. *Renal mobility*—Ligamentous attachments supporting and displacing renal fascia. Cylindrical body. Fatty capsule.

Muscular tone. Body position. Mobilizing force different from that affecting ureter.

b. *Ureteral fixation*—Attachments to peritoneum. Spermatic and ovarian veins. Free portion. Angulation—kinks. Mobilizing force different from that affecting kidney.

c. *Accessory structures*—vessels or bands. Valves, mucous membrane folds. May result in no harm but with increased mobility from trauma or other cause become obstructive factors.

2. *Active factors*

a. *Inflammatory*

Pyelitis

Ureteritis

Inflammatory stricture

b. *Traumatic*

Mobility increased

Hemorrhage

Scar

c. *Neurological*

3. *Direct factors*

a. *Obstructive (mechanical) factors*

Stricture; scar formation

Angulation (as in 1)

Pressure

Stone

b. *Motor insufficiency* or peristaltic failure.

c. *Urinary secretion*

The action of trauma toward producing a pyelectasis may be considered under the heads of: 1, Renal mobility; 2, ureteral fixation; 3, accessory structures; 4, hemorrhage; 5, scar formation.

V. RENAL MOBILITY

Increased mobility of the kidney occurs from variation of one of the several factors holding it within the limits of normal mobility but unless the ureter had some point of relative fixation or moved from forces acting in a different line from those affecting the kidney, no trouble would result.

The renal supports may be divided into, general, comprising body form, body position, muscle tone and peritoneal attachment; and, local, including more or less well defined and greatly variable ligamentous attachments to the liver, spleen, duodenum and pancreas; the renal fascia, the fatty capsule and the fine trabeculae holding this "fatty atmosphere" to the true capsule. Normal renal mobility within these supports is stated at 2 to 5 cm. (Kelly and Burnham). In a series of 48 post mortem examinations, I have found it to average 4 cm. on the right side and 4.5 cm. on the left. These observations were made on fresh cadavers by moving the kidneys within the limits of free mobility with the hand and measuring from a fixed point on the sacral promontory. Muscular action including that of the diaphragm; the forcing down of the colon or cecum or their ptosis by weight exert a greater pull than the weight of the normal kidney. It has been suggested that the increased weight of a congested kidney would add to this. However, the contained blood of such an organ in the early stage would not weigh over 25 grams which would hardly be a potent factor. Retained fluid within a dilated pelvis would be effective only after the sac had reached fairly large proportions. These two factors may be looked upon as results of the primary ptosis or inflammatory process and as such form a small part in a vicious circle but as primary factors should not be considered.

Body form and its relation to the renal position has received much study but the work of Wolkow and Delitzin (19) by the use of plaster casts has placed this factor on a tangible basis. The concavities or niches in which the kidneys rest are formed of the eleventh and twelfth ribs, the spine and flank muscles. These inverted pear shaped concavities have been shown by Becher and Lennhoff (20) to be absent clinically in the cylindrical shaped body. A body index was found by dividing the distance from the sternal notch to the pubis by the least body circumference and multiplying by 100. This serves to tabulate those cases in which renal mobility is predisposed to by body form. Harris (21) found this cylindrical body present in every one of 41 cases of movable kidney ascribed to trauma and believes that

the cylindrical body has more to do with moveable kidney than trauma.

The figures of G. M. Smith (22) regarding the lack of uniformity of the ascending and descending colic mesentery are of value as showing the great variation of the renal peritoneal covering. In the absence of a mesocolon the kidney involved lies adjacent to the posterior colic wall and is lacking in a part of its peritoneal covering, one of its important supports. Of 982 subjects Smith found the ascending mesentery present in but 30 per cent, the descending present in 37 per cent and both absent in over 50 per cent. In such cases the convergence of the anterior and posterior layers of the renal fascia below the lower renal pole of the kidney and their fusion with the connective tissue behind the ascending and descending colon is considered by Longyear (23) as forming a band or ligamentous structure capable of pulling down on the kidney when there is ptosis of the colon.

Displacement of the kidneys by traumatic violation of the above mentioned supporting factors can hardly be ascribed to a single trauma. The cylindrical body form, absence of the colic mesentery, and progressive decrease of the fatty capsule when associated with or followed by repeated muscular strain, with possibly an inactive heavy colon are factors which, when present over months or years, produce abnormal renal mobility. The single trauma in all probability but draws attention to a pre-existing condition.

The problem is analagous to so-called traumatic hernia, which is an acknowledged rarity, and is a result of congenital factors only contributed to by trauma.

VI. URETERAL FIXATION

Mobility of the ureter depends upon different factors from those causing renal mobility. If we imagine the ureter and kidney as a rigid body moved as such by the same forces, we cannot conceive of ureteral angulation. However, the kidney, and ureter are separate and distinct so far as attachments and so far as the action of mobilizing forces are concerned. The ureter being

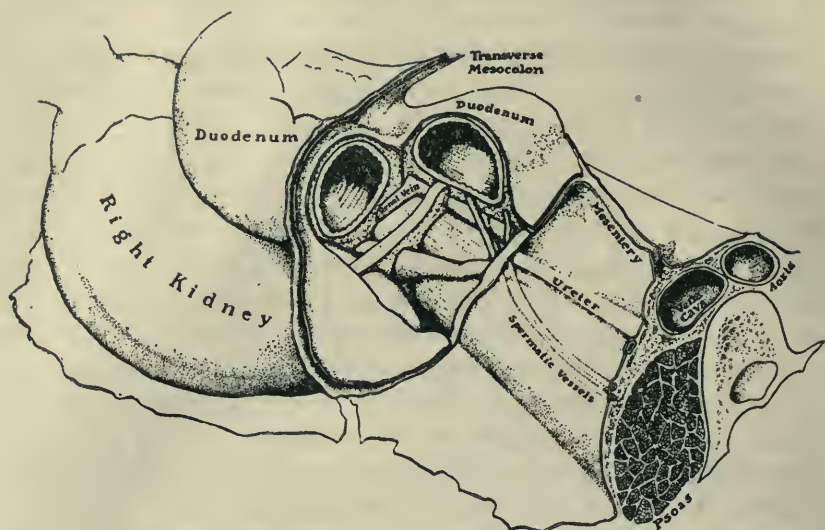


Figure 1

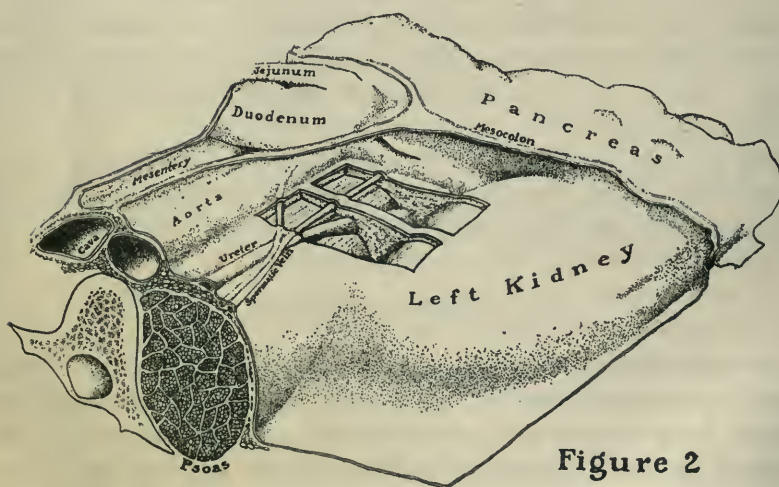


Figure 2

fixed to the peritoneum within 3 to 4 cm. from the mid-vertebral line, which is one of its most fixed points, is subject to peritoneal movements. The kidney imperfectly held by the above mentioned factors becomes abnormally mobile only when these are impaired. The kidney is normally subject to rhythmic motion with respiration and strain; the ureter moves with the peritoneum only and with that part of the peritoneum which is least mobile, i.e., that part attached to the midline. Between these two factors are the 4 to 5 cm. of ureter which, having left the peritoneum, passes through fat to the kidney. This mobile portion of the ureter is subject to angulation above its fixed point by renal mobility, hemorrhage and scar formation about it. In an attempt to localize a most uniformly fixed point 48 ureters were studied. In exposing a ureter the peritoneum was incised over it at the crossing of the iliac vessels. Here no fat was found between it and the peritoneum (figs. 1 and 2). The ureter was closely attached to the peritoneum. Passing upward the same condition existed until a point was reached, uniformly within a centimeter of the crossing of the spermatic vessels, where the ureter left the peritoneum and where fat was interposed between the two. With this most fixed point as an apex a triangle is formed by the ureter, the spermatic vessels and the renal vein. This triangle measured in an average on the left side 3.5 cm. to the renal sinus, 4 cm. to the origin of the spermatic vein and 4 cm. from the spermatic vein origin to the kidney. In subjects where any fat was present about the kidney within the renal fascia it is most marked about the renal sinus. On the right side the cava completes the mesial side of this triangle and its base is the length of the renal vein.

It seems to the writer that the apex of this triangle where the spermatic vessels cross anterior to the ureter is the most uniformly cephalad fixed point of the ureter and is the point where angulation is most readily caused by increased renal mobility, hemorrhage, or scar formation following hemorrhage or trauma. This point is included within the distance of least ureteral diameter, the upper isthmus of Schwalbe. The anterior layer of the renal fascia in some cases merges with the posterior

peritoneum toward the midline and below the lower renal pole. This structure offers further chance for fixation of the ureter. In one case a well marked passage of the ureter through this fascia was demonstrable.

In the type of pyelectasis under discussion the writer has considered the following chain of factors as expressing the probable stages of development.

1. Ureteral obstruction, periodic partial or complete, due to renal mobility acquired from trauma or strain.

2. Back pressure against renal secretion; injury to secreting mechanism.

3. Influence of blood pressure on renal secretion. Secretory pressure is about 70 mm. of mercury (Obinski, Starling, Henderson—quoted in Cushny). This is a varying factor and requires further study.

4. Entrance of infection with pyelo-nephritis and ureteritis which injure the renal parenchyma still further limiting secretion. Ureteritis most marked at the angulation with stricture formation.

1574. February 15, 1917. Female, age twenty-two years, single:

Has fallen a number of times while skating, producing a heavy jarring of the body. Two years ago while lifting a plank felt a severe strain and pain in the right flank. Has had pain off and on since this injury. One month ago acute attack of anuria and severe pain. Marked increase in frequency of urination. No hematuria, no calculi, no chills, nor fever.

Examination. Well nourished. General examination negative. Right kidney descends to the third degree on inspiration, very large, firm and tender. Left kidney lower pole barely palpable.

Cystoscopy. Ureteral openings uniform and normal. Functional capacity of the right kidney 19.5 per cent phenolsulphonophthalein, and the left 17 per cent. Pyelography showed a very large kidney on the right side with a marked angulation of the ureter at its entrance into the pelvis. The axis of the kidney in line with that of the body. Left kidney is much smaller.

Operation. Movement of kidney downward produces marked ureteral angulation. No accessory vessel found. Nephropexy.

Since operation three years ago patient has had no more trouble.

1145. June 30, 1913. Male, age twenty-six years.

Three years ago first had an attack of severe pain extending from the right flank to the bladder. This pain came on immediately after having strained in lifting, forcing the patient to stop work and lie down. On resuming his heavy lifting the pain recurred, requiring morphine to relieve. After two months, patient had slight pain off and on, when another severe attack followed resumption of his work. At this time appendectomy following diagnosis of appendicitis. Recurrence of pain on exertion after operation.

Examination. Well nourished. Chest and abdomen negative. Right kidney palpable and tender. Left kidney lower pole palpable.

Cystoscopy. Ureteral openings normal in appearance. No urine seen coming from right. Left opening contractile and urine coming from it. No. 6 catheter was obstructed about 23 cm. up the right side. On left side passed to the kidney. No urine obtained from the right side. Collargol injected by gravity caused severe pain and pyelography showed no solution entering the pelvis.

Operation by Dr. Hamann revealed a kinked ureter and dilated pelvis. The uretero-pelvic juncture was enlarged by the Heineke-Mikulicz technique, and nephropepy performed.

1444. December 6, 1915. Male, age nineteen years.

No serious illness. Played football for three years. During the second year was severely injured in left flank and confined to bed. Had a good deal of pain in the left flank extending to the bladder, pain severe coming on any time during the day, especially after heavy exertion, and always better on lying down. The attacks increased in severity, requiring morphine to relieve; no hematuria, no gravel. After the attacks he spoke of passing a large amount of urine.

X-ray for stone was negative. Urine contained a trace of albumin, no occult blood.

Cystoscopy. From the left kidney continuous flow, 25 cc. From the right kidney normal, periodic flow. Pyelography of the left kidney showed a marked hydronephrosis in such a position that ptosis from an obstructing band was almost certain.

December 13, 1915. At operation a large vessel was found going to the lower pole, the kidney pelvis markedly dilated, by reason of ptosis of the kidney obstructing the ureter over this vessel. Both the patient and his parents before operation expressed themselves as against any

palliative procedure and desired absolute relief from a single operation. Because of the size of the dilated pelvis, the kidney was therefore removed. Patient made a good recovery. Has been entirely free from pain since.

1295. July 21, 1914. Female, age sixteen years.

At nine years of age while lying in a sand pile a boy jumped with both feet, striking her in the left flank. Patient was in bed for a month following with severe pain. One year later began to have attacks of violent colic extending from the left renal region to the bladder. Has never had chills nor fever, no hematuria, no calculi.

Examination. Very well developed and nourished girl. Chest and abdomen showed nothing abnormal. Left kidney, lower pole palpable, markedly tender, both anteriorly and posteriorly. Head's kidney zone of cutaneous hyperesthesia markedly present.

Cystoscopy. Catheter passed to both kidneys. Functional test with phenolsulphonephthalein, right side 6 per cent, left side 37 per cent.

Pyelography showed a moderate hydronephrosis on the left side, no angulation of the ureter demonstrable, and a very large kidney present. No treatment accepted. Although this patient has been suffering from frequent severe attacks of pain she has now six years since examination had no recurrence, and has borne a child normally. Whether the inflation of the pelvis with collargol had anything to do with this I am unable to say, but I have seen a marked improvement of symptoms following pyelography in two cases.

1153. July 8, 1913. Male, age twenty-four years.

General personal history has no bearing on the case. At eight years of age patient fell from a tree, injuring the left side and back. Six years ago hematuria and had abdominal pain, but does not remember on which side. The pain was very severe and required morphine to relieve. Two months later had a recurrence of the pain on the left side extending from the kidney to the bladder, which was very severe and required morphine. No calculi passed, no hematuria. These attacks increased in frequency.

Three years ago after riding a horse, had a very severe attack and passed some blood. There were periods of intermission and relief was best obtained from recumbent posture. Attacks increased in frequency to every two to three days.

Cystoscopic examination showed the left ureter obstructed 23 cm. up, after which the catheter passed into the renal pelvis and 25 cc. of urine obtained by continuous flow. Pyelography showed the left ureter passing very close to the spine and opposite the kidney pelvis making a sharp right angle turn.

Operation refused.

1600. August 15, 1917. Female, age twenty-two years. Married, no children.

As a child had a severe injury to the right flank, nature of which is not clear. At seven years of age began to have marked bladder irritation, occurring irregularly. At twelve years of age had moderate arthritis in the shoulders, elbows, knees and ankles. From about this date began to have attacks of pain from the right flank radiating to the bladder and inner side of the thigh.

Examination showed a well nourished woman. Right kidney movable to the third degree, large and tender. Left kidney not palpable.

X-ray showed a very low kidney with angulated ureter, completely obstructing the entrance of thorium to the pelvis.

Cystoscopy. No. 7 catheter passed to both kidneys. The right showed functional capacity of 10 per cent phenolsulphonaphthalein and the left 17 per cent. Pure culture of colon from the right kidney.

Operation. August 14, 1917. No accessory vessel present. Kidney in very low position, extending to the iliac crest. No demonstrable cause for the angulation except position of kidney. Nephropexy.

December 9, 1919. Patient in perfect health, having none of her former trouble.

1541. July 26, 1916. Female, nineteen years of age.

At eleven years of age was thrown from a horse onto right side. Was also struck by the horse in the right flank just above the ileum. In bed for one week. Had scanty urine. Since this injury she has had repeated attacks of pain, beginning in the right flank and passing along the urinary tract. During these attacks marked increased frequency and recently chills and fever.

Six months ago appendectomy for same pain. Attacks recurred within one week after operation.

Examination showed well nourished girl, temperature 103°, tumor in the right flank the size of a small cocoanut, extremely tender.

Cystoscopy. Catheter could not be passed into the right kidney.

Emergency operation with drainage of the right kidney. Condition of the patient precluded its removal. Three weeks later removal of kidney which was a large infected pyelectasis. The size of the sac precluded determination of the exact location of the original ureteral obstruction, but that it followed the trauma and was a result of it is without question.

354. January 26, 1915. Male, thirty-seven years of age.

Fell from a wagon, striking on both hands and left flank on a rough road, walked to the hospital. Temperature 97°, pulse 60; marked pain and rigidity in the left flank; vomiting. Urine contained albumin and a large amount of blood. The first twenty-four hours 850 cc. of urine were passed. Patient reacted and temperature and pulse became normal. Treatment consisted of rest in bed, urotropin. Gross blood disappeared from the urine in three or four days.

Before the patient left the hospital a month later cystoscopy was done. Flow from both sides periodic. Ureteral openings look alike and normal. Three times as much urine coming from the right side as from the left. Phenolsulphonephthalein estimation showed 34 per cent from the right side, 12 per cent from the left. Color appeared from the right in two minutes, from the left in ten minutes. A pyelography was taken showing a well marked pelvic dilatation.

Patient confessed himself as feeling well and requested discharge.

About a year later re-admitted with a low grade right basal pneumonia and pleurisy, from which he rapidly recovered. He then gave a history of having had repeated pain in the left flank passing towards the bladder, and desired something done.

Cystoscopy. Catheter was obstructed on the left side at eight inches up. Functional test showed 42 per cent from the right, 3 per cent from the left.

Nephrectomy showed a large accessory vessel and band to the lower pole, over which the kidney had been forced down at the injury, producing an obstruction to the ureter and hydronephrosis.

The pelvis was dilated to about 50 cc. capacity. There was no evidence of its having been lacerated.

1363. April 22, 1915. Female, age forty-six years.

No serious illness. Four children living and well. Twenty years ago when four months pregnant fell against a stone step corner, striking heavily on the right flank. From that time she dates her symp-

toms, consisting of pain from the right flank to the groin; at times across the epigastrium, increased in frequency and severity, being especially worse after last pregnancy twelve years ago. Patient found that lying down and bending forward often relieved them. For these attacks of pain she was operated in the preceding four months for gall stones, appendectomy and finally a nephropexy without relief.

Cystoscopy and pyelography showed marked hydronephrosis on the right side (plate 4). The phenolsulphonephthalein excretion on this side was 9 per cent as against 24 per cent on the left side.

Nephrectomy.

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UROLOGICAL AND VENEREAL IDIOSYNCRASIES PRESENTED BY THE NEGRO¹

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In perusing the literature on this subject I have found numbers of articles on syphilis in the negro. So far only one has been found in which urological conditions have been considered and reported with statistics. In 1896, Matas (1) reported a series composed of his findings from 1884 to 1894. Since then, so far as I can find, no similar comparison has been published.

We shall attempt to show the individual peculiarities of urological and venereal diseases as existing, black against white, from the records of the Louisville City Hospital and from several camps where large numbers of colored troops were quartered. For comparative interpretation of our statistics we have grouped our cases thus:

1. Every patient, white and black, admitted to the urological department² of the Louisville City Hospital from June 1, 1916, to April 1, 1920.

2. Dispensary patients composed entirely of venereals, Stockade Infirmary, Camp Pike, Arkansas, and Camp Alexander, Port of Embarkation, Newport News, Va.

In group 1 are routine hospital cases from Louisville and vicinity, while in group 2 are dispensary conditions represented by almost every state in the South, showing an average which I accept as a criterion to the general rate of infection among the negroes. At Camp Pike white men and negroes were segregated in a stockade with forced treatment and complete rest, while at the Venereal Hospital, Camp Alexander, all patients were colored and doing full duty while under treatment.

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The diseases more prevalent among the white men are: hydrocele, varicocele, epididymitis, prostatitis, prostatic hypertrophy, malignancy, calculus, kidney infections, arthritis (gonococcus), syphilis and neuro-syphilis. Those more prevalent among the negroes are: stricture, urinary extravasation, fistula, periurethral abscess, lesions of extragenitals, and lymph-adenitis.

Our experience is, and our statistics appear to show, that complications are more often observed among the white men. It is

TABLE 1
Findings in group 1

	NUMBER OF CASES			PERCENTAGE OF ACTUAL PREVALENCE	
	Total	White	Black	White	Black
Hydrocele..	20	13	7	65.0	35.0
Varicocele..	28	28	0	100.0	0.0
Epididymitis..	77	48	29	62.3	37.7
Prostatitis..	11	8	3	71.0	29.0
Stricture (urethra and ureter)..	76	32	34	41.0	59.0
Prostatic hypertrophy..	38	30	8	70.0	30.0
Malignancy (kidney, bladder, prostate, extragenitals)..	16	10	6	60.0	40.0
Nonspecific lesions of genitals..	15	5	10	33.3	66.7
Lymphadenitis..	37	13	24	30.0	70.0
Calculus (kidney and bladder)..	4	3	1	75.0	25.0
Kidney (tuberculosis, pyelitis, pyonephrosis, hydronephrosis)..	15	11	4	70.0	30.0
Arthritis (gonococcus)..	25	19	6	76.0	24.0
Cystitis..	31	20	11	64.0	36.0
Syphilis (one year)..	120	90	30	75.0	25.0

rather difficult to explain this when it is agreed that infection among the negroes is quite universal; that the living conditions are far beneath the white, and that medical attention is usually of the passive type.

The average negro cannot be impressed with the seriousness of his condition, nor can he be made to understand that he must coöperate in reporting to the outpatient department for further treatment after his discharge from the hospital. He is primarily interested only in subsidence of symptoms and relief from pain,

after which he returns to his former environments, reporting to the hospital only when pain persuades him that attention is necessary.

Why varicocele is so very infrequently observed in the negro is rather difficult to explain. I do not recall a single case in which operation was performed in my experience of fifteen years service at the Louisville City Hospital. Hydrocele, epididymitis, prostatitis, stricture, lesions of the genitals, arthritis and cystitis I shall discuss later.

As to the adenomatous prostate, I am not in accord with Matas when he says that according to his statistics hypertrophy of the prostate in negroes appears to be *more* frequent and operation *more* fatal in individuals of this race. We found it decidedly *less* frequent and *less* fatal.

Clark (2) cites the fact that an enlarged prostate in a negro is a very rare affection, and that this is the more remarkable when one considers that it is a fibroid condition, and that the female negro is especially prone to fibroid disease of the uterus. He gives as a reason for this immunity from enlarged prostate the fact that but few negroes reach the age at which this gland usually begins to cause trouble, say about fifty-five years.

If we agree that fibrosis is more marked in the negro than in the white man following injury to fibrous tissue either by chemical (bacterial) or mechanical agents—as evidenced, for example, by the keloid formation that is observed almost exclusively in negroes—then would it not be reasonable to expect that we might find a similar tendency toward fibrosis in the prostate of the negro following chronic prostatitis? Such, however, is not my experience.

In malignancy of the kidney, bladder, prostate and extragenitals, the percentage is slightly higher among whites.

Calculus, while not rare, is rather in the minority in the negro, the ratio being 75 per cent in the white men to 25 per cent in the negro.

Kidney infections, other than tuberculosis, are rather infrequent in the negro, although pyonephrosis and pyelitis are occasionally observed. Colon bacillus and gonococcal infections of the kidney are quite rare.

The outpatient department or dispensary cases present quite a different picture. It is my belief practically all negroes are venereals. Why this is true is quite easily understood. Furthermore, it is my belief that comparatively few are ever cured of venereal disease. When an occasional one is cured, he betakes himself to his usual haunts to become quickly reinfected. I am convinced that the majority of negroes do not respect the moral code or honor the sanctity of wedlock; so the endless chain of infection and reinfection goes merrily on,

During my service in the army I had occasion to observe many hundreds of these cases. At the Stockade, Camp Pike, there were at one time 4400 cases, of which 1400 were among white men and 3000 among negroes. The white men were of the usual types, while the negroes possessed all of the classical conditions and many additional ones.

At Camp Alexander, where many hundreds of cases were observed and studied, I was finally convinced that the negro possessed many characteristics quite unlike the white man, and that the routine treatment usually indicated not only did not improve his condition but actually made him worse. As an example: almost without exception negroes with chronic urethritis also had stricture or fibrosis of greater or less degree; and when dilatation was attempted, an increase in the fibrosis was noted. This reaction or increased fibrosis did not subside but rather increased in severity as treatment was applied.

The number of negroes coming to operation for urinary extravasation is very high, and the ultimate prognosis is grave. The ratio is four negroes to one white man. Fistula, as a rule, is coincident, and many are noted with complete obliteration of the urethra, the canal being completely closed by cicatricial tissue. Such patients will void for many years through these fistulas, and it was noted that many gave the history of not remembering when they had voided through the urethra. Typical of the race, they are brought to operation ordinarily as emergencies, deeply toxic and traumatized, so that the mortality rate is unusually high.

Periurethral abscess is also very prevalent, the ratio being decidedly higher among the blacks.

It is my experience that acute prostatitis, acute posterior urethritis and cystitis are more infrequent. It was also noted that in chronic urethritis the prostate was rarely involved, especially was this true in the pure negro.

Among lesions of the extragenitals, many hundreds of ulcers were noted which were neither syphilitic nor chancroidal. Numbers of the men gave the history of having had these ulcers for many years, the majority being uninfluenced by treatment. By laboratory investigation all were proved to be negative for micro-organisms and malignancy.

Thompson (3) says that at Camp Dodge, with but few exceptions, every negro that he saw for venereal disease of any kind had a general adenitis of some degree.

Lymphadenitis was noted in the majority of negroes with syphilis, chancroid or gonorrhea. A considerable number were noted with enormous inguinal enlargement following exercise or a strenuous "hike." Many of the latter types would after a time "break down" and suppurate, resembling the typical bubo of chancroid.

Inguinal adenitis in the white man is rather rare in gonorrhea, but it was noted that the majority of negroes with an active discharge presented marked lymphadenitis.

Various authorities agree that syphilis is more prevalent among negroes than whites.

Jones (4) states that the high mortality of pulmonary tuberculosis in the black race is due to the damage wrought by syphilis. He feels justified in assuming from his experience that 75 per cent have syphilis. My observations tend to confirm this statement. While I do not agree that the negro is more susceptible to syphilis, I believe that he begins sexual life at a much earlier time than the white man, and also that the negro is more active sexually, so that the combination of environment and prevalence of venereal disease render the ratio of infection much higher. Comparing the earlier lesions of syphilis, I found very little difference, as both respond equally to treatment.

IMPRESSIONS

The average negro as seen in wards and clinics is a child of the moment, irresponsible and at all times optimistic. He is born amid infection, is infected usually throughout life, and succumbs eventually in spite of it rather than directly from it. He is observed usually a syphilitic, a living culture of gonococci, a walking clinic as it were. The average male is usually a splendid specimen of physical perfection. He accepts with stolid indifference the grave prognosis and assents to treatment only in the event pain makes it imperative to do so. When relieved, he disappears to appear and reappear as many times as discomfort interferes. And with all the neglect, with unhygienic surroundings and poor food, he appears to go along very well.

We find that the white man, with everything in his favor, has more complications with the exceptions of stricture, lesions of the extragenitals, and lymphadenitis. Why this is true is indeed a question. Can we say it is environment? Surely not. Heredity? Very questionable. Then what is it that acts as a charm and protects the negro from so many venereal sequelae and gives him in their stead the enlarged glands, the fibrosed urethra, and ulcers of the penis in such profuse abundance?

Why is it that the negro with chronic gonorrhea of many years' standing, indulging in every excess possible meanwhile, is found on examination in almost every instance to have stricture of the urethra with some of its complications? Why is it that in these chronic infections the prostate is usually found normal in size, contour and with so little infection present? And if the prostatic secretion be cultivated, only a few staphylococci will be found? This was noted the rule in the majority examined. Again, massage of the prostate produced, after several séances, a negative smear.

Is the negro more susceptible or does he have a relative immunity against certain venereal diseases? It is my belief that he is neither more susceptible nor is he immune to many of the complications; but as Matas (1) has said, he could not offer a satisfactory explanation of these apparent exemptions from many

of the complications, unless it be that the virulent effect of the gonococcus is chiefly expended upon the epithelium of the urethra, which desquamates sufficiently to expose the connective tissue substratum of the mucosa and thus brings into relief the fibroid tendency of the negro. With this I am in complete accord. It may be that the mucosa of the anterior urethra is peculiarly adaptable to the requisites of the gonococcus; that the attack on the anterior urethra is so active that when fibrosis occurs the remaining virus is not diffusible in that further extension and infection is not possible; that the virus as existing in the anterior urethra is virus which is absorbed by the lymphatics, and the micro-organisms themselves are inert so far as further infection is concerned. If this be true, then the tendency toward adenitis is easily understood, and instead of the negro's being immune from complications, he has a keloid tendency in the urethra which is a blessing in disguise, an idiosyncrasy of inestimable value.

It is undoubtedly true, as recorded by Quartrefages (5) that "unity of species and multiplicity of races involve the liability of all men to common diseases which will, at the most, vary as to accessory phenomena; but also allow the existence of diseases more or less peculiar to certain human groups."

During the last seventy-five years, many changes have occurred to modify the aptitude of the negro toward diseases in general and venereal diseases in particular. The environment is an entirely different one; he has gradually lost his immunity toward certain diseases, and on assuming the vices of the white has fallen heir to many additional ones.

In the interval between the reporting of the statistics of the Charity Hospital, New Orleans, in 1896, and the present time, a period of twenty-six years, quite a change has occurred.

In table 2 it will be noted that of the twelve urologic and venereal conditions reported, in every instance, or 100 per cent, actual prevalence was higher among the white men. In those of the Louisville City Hospital, of fourteen reported, in eleven the greater prevalence was among the white men and in three the percentage was with the negroes. Therefore, in comparing the

statistics of the Charity Hospital twenty-six years ago with our statistics of the last four years, it is found that against the ratio of 100 per cent we have one in which 78 per cent are found in the white men.

TABLE 2
Change occurring in twenty-six years

	CHARITY HOSPITAL NEW ORLEANS, 1884-1894		CITY HOSPITAL LOUISVILLE, 1916-1920	
	White	Black	White	Black
	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>
Hydrocele	62.96	37.04	65.0	35.0
Varicocele	None recorded		100.0	0
Epididymitis	71.0	29.0	62.3	37.7
Prostatitis	66.66	33.33	71.0	29.0
Stricture	54.67	45.24	41.0	59.0
Prostatic hypertrophy	58.9	41.1	70.0	30.0
Malignancy*	68.0	32.0	60.0	40.0
Nonspecific lesions (chancroids only) (geni- tals)	65.29	37.71	33.33	66.66
Lymphadenitis	80.0	20.0	30.0	70.0
Calculus†	76.74	23.26	75.0	25.0
Arthritis (gonococcus)	73.9	26.1	76.0	24.0
Kidney (tuberculosis, pyelitis, pyonephrosis, hydronephrosis)	None recorded		70.0	30.0
Cystitis	71.62	28.38	64.0	36.0
Syphilis‡	56.89	43.11	64.0§	36.0§

* All malignancies wherever found.

† Bladder calculi only.

‡ All types, primary, secondary and tertiary.

§ All types (Department of Dermatology, University of Louisville), primary, secondary, tertiary and neurosyphilis.

CONCLUSIONS

1. The ratio of venereal disease is much higher among negroes.
2. Complications, other than stricture, lesions of the extra-genitals and lymphadenitis, are more numerous among the white men.
3. Stricture is general among negroes, and is due to the keloid or fibrosis tendency.

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PHYSIOLOGICAL AND PHARMACOLOGICAL STUDIES OF THE PROSTATE GLAND

III. EFFECT OF PROSTATECTOMY ON THE BEHAVIOR OF ALBINO RATS

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INTRODUCTORY

The recent advances in our knowledge of internal secretions have caused not only physiologists but also clinicians to be on the lookout for manifestations pointing to a possible derangement in the functions of various glands. To this the prostate gland is no exception. There is an increasing tendency to regard the prostate gland as possessing an internal secretory activity as well as an external one, and a multitude of symptoms noticed in the course of prostatic diseases on the one hand and the sequelae after prostatectomies on the other have been sometimes ascribed to the lack of such a hormone.

Among the commonest symptoms of such a character that have been correlated with an internal secretion of the prostate gland are various manifestations of a psychopathic or neuropathic type. Thus Guisy (1) in an interesting monograph gives some very interesting data on the subject. He found among 31 cases of prostatic hypertrophy in patients between fifty-seven and sixty-seven years of age, 3 subjects exhibiting psychopathic disturbances of the hallucinatory and melancholic type. Out of 7 cases of prostatic cancer, 1 patient was found to suffer from melancholia and optic hallucinations. Among 4 cases of tuberculosis of the prostate the same author found also 1 man suffering from cerebral depression. Guisy further states that he encountered 2 cases with profound depressive psychoses among

17 patients in whom complete prostatectomy had been performed some time previously, and the same author quotes statistics from other writers who have also noted psychic disturbances after transvesical prostatectomy. Similar experiences are reported by Rovsing (2), Voelker (3), and Rumpel (4). On the other hand, probably the vast majority of urologists are inclined to the view that complete extirpation of the prostate gland has no bearing on the character and mental efficiency of the patients, and others such as Freyer and Ertzbischoff (5) go even so far as to state that, on the contrary, they have often known psychopathic patients to improve in health of body and mind after prostate operations.

It is obvious that clinical data are very unreliable in drawing conclusions as to the relationship of prostatic disease or extirpation of the prostate and the changes in character, mentality, and neuromuscular coördination of the patients. In the first place, the extirpation of the prostate is performed generally in men of advanced age who may already have been suffering from various senile pathological changes. In the second place, any alteration in the health of the patient may very justly be ascribed to the shock of the none too gentle operation. Again, the anesthetics may well bear some responsibility for the after effects. Lastly, the occurrence of psychic disturbances in the patients may be ascribed to a variety of other causes or may even be purely a coincidence. Thus for instance, one reads with a smile the statement of Guisy, that he found 4 cases of melancholia among 51 patients suffering from acute gonorrheal prostatitis.

METHOD OF APPROACH

Perhaps the most satisfactory method of approaching the question of the relationship between an internal secretion of the prostate and the mental efficiency of an individual is to study the effects of the complete extirpation of the prostate on the functions of lower animals. An attempt in this direction has been made by the authors in the present investigation. The most suitable animal for use in conducting such experiments is

the rat. This little rodent possesses a prostate gland which can be easily and completely extirpated. Furthermore, the prostate of the rat is enormously large in proportion to the weight of the animal when compared with that of man. The authors have often removed prostates from rats which weighed as much as one four hundredth of the weight of the whole animal. If we assume the weight of an average man to be 70 kilos and the average weight of the human prostate to be 20 grams, the ratio between the weight of man to the human prostate is 3500 to 1, a figure very small in comparison with that of the rat (400 to 1). It is therefore fair to assume that if the prostate gland elaborates an internal secretion, the complete extirpation of that gland in the rat would lead to much more greatly accentuated disturbances than a similar operation in man. Furthermore, the effects of prostatectomy in rats can be studied in perfectly normal and young adults; so that it may be possible to exclude the effects of senility and other pathological changes which must always be taken into consideration in making deductions from clinical data. The position and size of the prostate gland has been well described by Walker (6), whose plate is here reproduced with his permission (fig. 1).

The authors accordingly selected a number of healthy young adult male rats and performed complete prostatectomies on them. The behavior of these animals was studied before and after the operations and in this way the effects of prostatectomy on the neuromuscular and cerebral efficiency of the animals was investigated. The most convenient method for the study of such phenomena was by the use of a circular maze, such as has been invented by Professor Watson of the Psychological Laboratory of this University. This apparatus is described in detail as follows.

DESCRIPTION OF THE MAZE

The circular maze shown in figure 2 is made with wooden base and aluminum walls. The base is 150 cm. in diameter and 4 cm. in thickness. Its upper surface is marked off by grooves into a series of concentric circles. The diameter of each of the

circles is as follows, beginning with the outermost one: 140 cm., 120 cm., 100 cm., 80 cm., 60 cm., 40 cm., and 20 cm. Into the

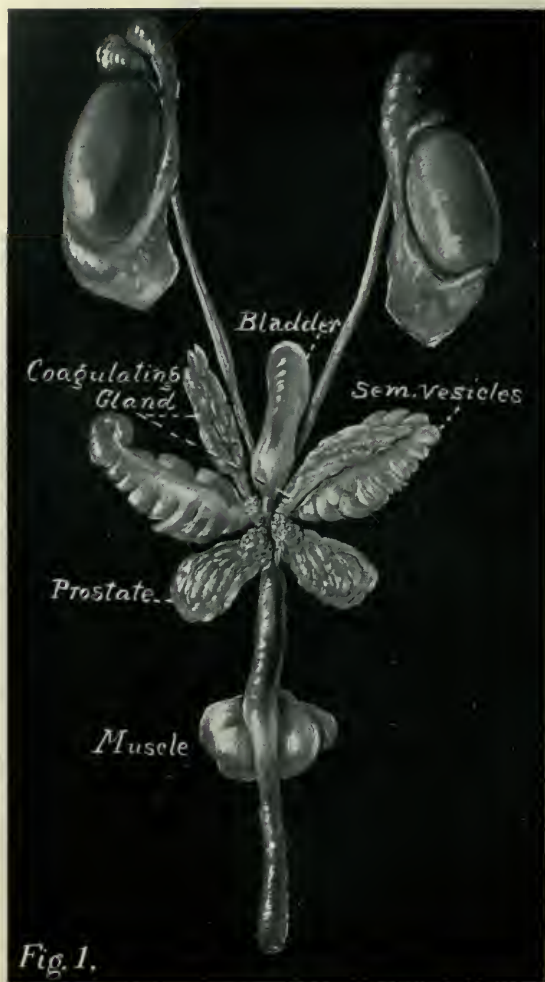


FIG. 1. GENITO URINARY ORGANS OF THE RAT, SHOWING PROSTATE GLAND, ETC.

After Walker; by permission of the author and publishers

circular grooves are inserted sheets of aluminum 18.5 cm. high and 0.8 mm. thick. Each strip of aluminum is cut just 10 cm. shorter than the length of the circular groove into which it is to

be fitted, thus giving an opening into the alley. By means of this arrangement it is possible to slide the aluminum around its groove and thus to place the entrance in any desirable position. In the present investigation, the openings or entrances to the alleys were placed in the position indicated in figure 1, there being 7 openings so arranged that the rat had to make alternate turns and left, in the order indicated by nos. 1 and 7. In



FIG. 2. CIRCULAR MAZE

addition to the doors or openings, the alleys are provided also with obstructing partitions, which form a number of blind cul-de-sacs. A wire screen half of which is shown (*W*, fig. 3), prevents the animals from crawling over the top.

The camera lucida attachment invented by Professor Watson is illustrated in figure 3. A large plate-glass mirror *M*, 91 cm. wide and 121 cm. in length, was placed at an angle of 45 degrees,

directly over the center of the maze. At a certain distance from this mirror a second mirror, M , 60 cm. by 75 cm., is placed at an angle of 45 degrees above the maze, at such a distance from

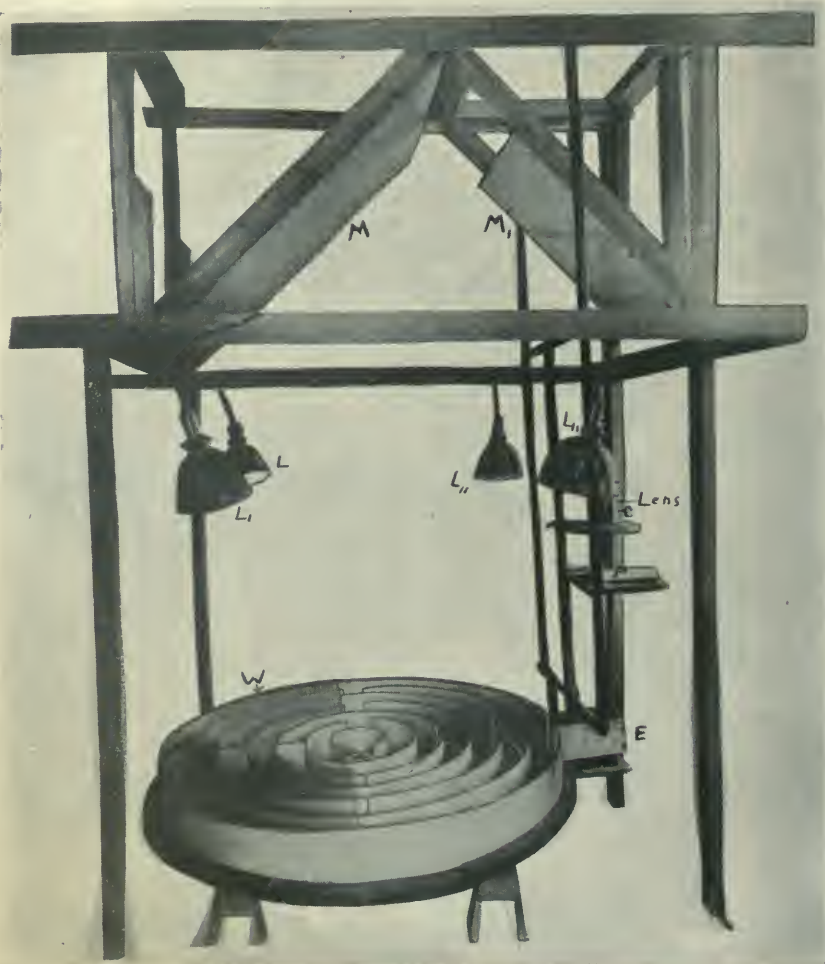


FIG. 3. CIRCULAR MAZE WITH CAMERA LUCIDA ATTACHMENT

the first mirror that the light reflected downward from it falls outside of the maze. Below M , and in the light reflected from it, is placed a single achromat, 6 cm. in diameter and 50 cm.

focus. The lens is placed in a barrel and the barrel is attached to a wooden disc 30 cm. in diameter. This board is attached to an iron collar which slides freely up and down and gives a very easy means of adjusting the size of the image. A circular piece of paper is laid upon a wooden shelf, below the lens, and the distance is so adjusted that the reduced image of the maze is focused upon the paper. Extraneous light is excluded by means of a soft dark flannel curtain, not shown in the figure. As may readily be seen from the figure, the maze must be illuminated quite highly in order to produce a clear image. This illumination is obtained by means of four powerful electric lamps, with opaque shades placed symmetrically around the maze. By means of the camera lucida attachment, the movements of an animal in the maze can be traced upon white paper with a soft pencil. Such tracings are especially useful in the study of the learning of the maze problem, such as has been done by Miss Hubbert and others. In the present investigation, where the effect of drugs on the behavior of the animals was studied after the rats had been trained, the use of this attachment was not essential and it was therefore dispensed with in a great many of the experiments.

The study of the behavior of the rats in the circular maze is begun by placing an animal in the center of the maze and feeding it from the bowl *F* for three successive days. During these three preliminary feedings, which last from ten to fifteen minutes, the entrance 7 is blocked off, so that the animal may not roam around. On the fourth day, the rat is placed in the cage *E*, then the trap-door *T* is raised and the animal allowed to enter the first alley. The animal then gradually learns to find its way to the center of the maze, when it is taken out and the experiment is repeated. Generally three trials are made on each day. For work with the maze, albino rats, which are very tame must be employed. The animals must be handled gently with the hands and under no circumstances must they be picked up with forceps or similar instruments. The most suitable animals are found to be rats approximately sixty to ninety days old. Older animals are apt to be sluggish while very young

rats do not learn the maze problem so readily. Ordinarily the albino rats learn the maze problem in about two weeks, and sometimes within a shorter period of time. An animal is considered to have solved the maze problem when it has learned to find its way into the center of the maze by the shortest route, that is, without any errors, on three successive trials. The technic of training is described more in detail by Hubbert (7).

ANALYSIS OF THE DATA FURNISHED BY THE MAZE

The maze problem enables the psychologist to study the mode of learning of a rat. In studying the effect of drugs, the maze problem can be utilized in two ways. Animals may be subjected to the influence of drug action first and then trained in the maze with the purpose of ascertaining the effect on the rate of learning. Again, animals may be first taught to solve the maze problem and then the effect of a drug is studied in reference to its influence on their behavior, memory-habit, etc. Furthermore other data can be obtained from the maze, after administering drugs to rats, which may show the effect on neuromuscular coordination, and various somatic changes. As to exactly what the mechanism of learning the maze problem may be, the explanations given by various psychologists differ widely. Among the hypotheses which have been advanced to account for the reintegration of conduction paths in learning, there are at least three which stand out as rather opposed to one another in respect to the neural processes which they imply (8). The hypothesis suggested by Ladd and Woodworth (9) assumes inhibition of successive activities as the fundamental process which results in the selection and fixation of random activities. The second hypothesis, given by Angell and others (10), assumes nervous reinforcement as the fundamental process by which successive acts become linked together in habit-formation. The third hypothesis (Watson, (11) depends chiefly upon the chance spreading of nervous excitation, or the simultaneous activation of two afferent pathways in such a way that the final common part of one is able to divert the discharge of the other and so

bring about a permanent connection between itself and this afferent path. These hypotheses by no means exhaust the theoretical considerations of the maze problem (Dashiell (12)). For the study of drug action, however, the various theoretical considerations are of secondary importance and the data obtained are of a much more definite nature, as will be seen from the following exposition.

EFFECT OF PROSTATECTOMY ON MEMORY HABIT

Two series of experiments were conducted by the authors. In one series the animals were first trained to solve the maze problem and after having acquired perfect facility in doing so the same animals were prostatectomized and their subsequent behavior studied. In another series of experiments a number of rats were first prostatectomized and then allowed to recover completely from the effects of the operation. They were then left alone for a considerable number of weeks in order to permit a deficiency in the internal secretion of the prostate (if there be any) to manifest itself. Finally these animals were trained in the maze and their rate of learning was compared with that of a series of control rats which were either not operated at all or which underwent the operation of laparotomy but without the extirpation of the prostate.

In the first series of experiments six young, adult, male albino rats were trained in the circular maze. After the animals had learned to run through the maze by the shortest route in the shortest period of time without committing any errors, they were etherized and the complete extirpation of the prostate gland was performed on each rat, under aseptic precautions. The wounds were then closed and allowed to heal and the animals were left undisturbed in their cages for sixteen days. Two other rats were trained in the maze in exactly the same way and after having learned the problem were also etherized and operated on. In this case however, a laparotomy was performed and the various organs examined but no prostate gland was removed. The incision then was closed and the animals allowed to recover

and were used as controls. On the seventeenth day both the prostatectomized rats and the control rats were put in the maze and their behavior was studied. It was found that all the rats retained their memory and ran quickly to the center of the maze without committing any errors, even though they had not practised in the apparatus for sixteen days. On the following, or eighteenth day, all the rats were again put through the maze and were found to have recovered completely their original normal behavior. They ran through the maze by the shortest route in the shortest period of time without making any mistakes, just as if they had not been operated upon. No difference in behavior or effect on the memory-habit between the prostatectomized rats and the control rats was noticed.

EFFECT OF PROSTATECTOMY ON THE RATE OF LEARNING

In this series of experiments a total number of 34 rats were used. Of these 6 rats were studied by Macht and Mora but the record of the experiments was lost. The results, however, agreed completely with those obtained in the 28 rats used in the experiments by the present authors. Fourteen of the animals were prostatectomized. In performing this operation the animals were given ether as an anesthetic and antiseptic precautions were observed. Great care was taken to remove the prostate completely. After the operations the wounds were closed and the animals were allowed to recover. In each case the wounds healed satisfactorily. The other 14 rats were used as controls. Of these 8 were operated on, a laparotomy being performed and the bladder and prostate being handled and examined but *not* excised, so as to subject the animals to as much operative shock as the prostatectomized ones. The 6 other animals were used as unoperated controls.

All of the animals were left undisturbed in their cages, without training, for periods of time ranging from five to nine weeks. After this prolonged rest, training was begun and observations were made on the rate of learning the maze problem. The animals were put in the maze 6 times a week and wherever possible three successive trials were given each rat, on each day.

When the animals, however, were sluggish, in a few cases only two trials were made on some days. The results obtained are exhibited in table 1.

It will be seen that the average time of learning the maze in the case of the prostatectomized rats was 8.2 days and this represented the average number of 22.7 trials. The average time of learning the problem in the case of the control rats was 9.9 days, representing an average of 25.8 trials. The operated and unoperated controls were averaged together as little difference was found between the two.

TABLE 1

PROSTATECTOMIZED RATS			CONTROL RATS			
Rat number	Trials to learn	Days to learn		Rat number	Trials to learn	Days to learn
I	31	11	Laparotomy only	A	29	12
II	40	15	Laparotomy only	B	19	8
III	52	18	Laparotomy only	C	23	9
IV	18	8	Laparotomy only	D	30	12
V	36	12	Laparotomy only	E	12	4
VI	15	7	Laparotomy only	F	22	9
VII	16	6	Laparotomy only	G	38	14
VIII	12	4	Laparotomy only	H	21	8
IX	12	4	Unoperated control	I	18	7
X	18	6	Unoperated control	J	21	8
XI	15	5	Unoperated control	K	38	15
XII	12	4	Unoperated control	L	32	12
XIII	22	8	Unoperated control	M	31	11
XIV	19	7	Unoperated control	N	37	10
Average	22.7	8.2		Average	25.8	9.9

A comparison of the figures obtained reveals the interesting fact that the rate of learning after prostatectomy was *not impaired* and was just as good as in case of the control rats. Indeed if any differences were to be noted it would seem that the prostatectomized rats learned a little more quickly than the control animals.

DISCUSSION

The authors studied the effect of prostatectomy on the rate of learning on the one hand and on the memory-habit and general behavior on the other. The data obtained in both

series of experiments show no difference between the prostatectomized and nonprostatectomized rats. It is to be born in mind that in this investigation young adult males were used; thus excluding the possible effect of senile changes. Again in both the prostatectomized and the control animals care was taken to produce the same amount of surgical shock so that any difference due to such a cause might be eliminated. Furthermore, in choosing the control animals the authors have taken pains to select rats of approximately the same ages. Lastly, the effect of anesthesia was the same in both cases so that any changes produced could not be ascribed to the ether. This, however, was unnecessary inasmuch as Macht and Mora (13) had previously studied the effect of anesthesia on the subsequent behavior of rats and found that ether produces no changes in the behavior of the animals. The above experiments therefore, lead to the conclusion that if the prostate gland possess an endocrine function, its internal secretion bears no relation to the mental efficiency of the animal; in as much as prostatectomized rats behave in all respects the same as the rats which were operated on but in which the prostate was left intact. The conclusions derived from the present research agree with the experiences of the majority of urological surgeons in general and with the experience of the surgeons in the Brady Urological Institute, in particular.

SUMMARY

1. The effects of prostatectomy were studied on albino rats in the circular maze.

2. In one series of experiments the effect of prostatectomy on the rate of learning was investigated.

3. In a second series of experiments the effect of prostatectomy was studied in relation to behavior and memory-habit.

4. It was found that in both series of experiments no difference in the behavior between prostatectomized and control rats occurred.

5. These observations lead to the conclusion that the endocrine function of the prostate gland bears no relation to the mental efficiency of the animals.

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VAS PUNCTURE AS A MEANS OF CURE FOR CHRONIC SEMINAL VESICULITIS: A REPORT OF FIFTY-FIVE CASES.

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The problem of caring for cases of chronic gonorrhea in the army, while somewhat different from a similar one in civil life and private practice, constitutes a large part of the work of urologists in general hospitals. The soldier finds the complaint and show, of a morning drop, or of any one of the familiar signs of chronic gonorrhea, an easy and unfailing pass to a tour of light duty, and often after failure to keep up treatment ordered, an open door to the post hospital, or nearby general hospital.

Once inside the hospital, he begins to enjoy the privileges of the institution, and would rather continue a patient than return to duty. This fact encourages him again to neglect treatment, or if apparently cured, to procure a return to the hospital and friends made there, having produced again for his medical officer some telltale sign of persistent infection.

During a period of six months, a dozen or fifteen infantrymen, from a nearby station, spent an aggregate of ninety days each, in hospital, rarely if ever confined to bed, usually too intractable to confine to wards, except under guard, each having been returned to duty repeatedly, with negative prostate secretion, normal genitalia, cured urethra and clear urine.

A large percentage of chronic gonorrhea cases have persistent involvement of the seminal vesicles and of the prostate; the prostatitis will improve with massage; proper massage of the vesicles is difficult and often impossible. At best, massage simply improves the circulation of these structures, and does not empty them of diseased secretion and detritus. Other

treatment of chronic vesiculitis, has as its aim, direct application of some medicament, to the inner surfaces of the vesicles themselves. Using Dr. Greenberg's catheterizing cysto-urethroscope, it is possible to catheterize the ejaculatory ducts, and inject the desired solution; Dr. Hugh Young has devised a two-pronged catheterizing instrument with which he catheterizes the ejaculatory ducts through a simple urethroscope. The practical application of these methods of treatment is difficult, and any solution injected into the ejaculatory duct must of necessity force the vesicular contents backward. Another method of direct application of treatment to the vesicle, is that of Dr. Belfield, who by means of vasotomy or vas puncture, injects a solution into the vesicle in the direction in which the vesicle normally empties itself.

Vas puncture is indicated in the following types of cases:

1. Cases with persisting or recurring epididymitis, with chronic seminal vesiculitis, which have resisted other treatment.
2. Cases with acute vesiculitis, especially if there is a beginning arthritis.
3. Cases with chronic vesicular involvement, with co-existing arthritis.
4. Optional cases having recurring urethritis, but no palpable evidence of vesiculitis, and no evidence of a focus within the urethra.
5. Cases with recurrent urethritis, without focus in the urethra, and chronic prostatitis and seminal vesiculitis.

Vas puncture is contraindicated in the following types of cases:

1. Cases with acute epididymitis.
2. Cases with acute anterior urethritis.

Vas puncture, with one or more injections of a solution of collargol, or other suitable medication, promises improvement or cure in a large number of cases, especially of those with disease confined to prostate and vesicles. Gonorrheal arthritis is also amenable to this treatment, with eradication of the focus of infection and immediate abatement of arthritis, as indicated by striking results in some of the cases reported in this series.

As an operation, vas puncture is simple and yet difficult. One can not have too much skill, or too intimate a knowledge of the anatomy of the cord structures, and of the vesicles, for success in this mode of treatment.

Indebted to Dr. Belfield for popularizing and proving the value of vas puncture, we naturally look to him for technique. In the Journal of the American Medical Association, issue of January 17, 1920, there is an admirable account of the use of vas puncture for acute seminal vesiculitis, which the author claims is an accompaniment of a large number of cases of acute urethritis. In his article, just referred to, Dr. Belfield describes minutely, his technique for vas puncture as well as for vasotomy, with illustrations.

The technique we have used at Walter Reed United States Army General Hospital, varies somewhat, but in principle, is the same as that of Belfield. It must be distinctly understood that the two operations, vas puncture and vasotomy, are entirely different. Vasotomy involves not only the isolation of the vas, but also a real opening of its lumen, with its attendant dangers of infection and stricture and sinus formation. Vas puncture consists of a simple puncture of the slender tube with a fine needle, allowing injection of a medication without in any way compromising the lumen.

Puncture is best done about midway between the epididymis and external ring. After localization of the vas in the cord structures, the local anesthetic is injected around the site of proposed incision, without letting go of the vas. The incision is best made on the most anterior surface of the scrotum, away from that part more subject to moisture, and less readily dressed. The incision, half an inch in length, may be made in either direction; a clean cut through skin and dartos exposes the cord structures which press up into the wound. The vas is then isolated; this is best done by stripping the covering structures in the longitudinal direction, along the axis of the cord. We feel that the most essential point is to completely bare the vas for the distance of one inch at least. See figure 1 as an illustration of this step.

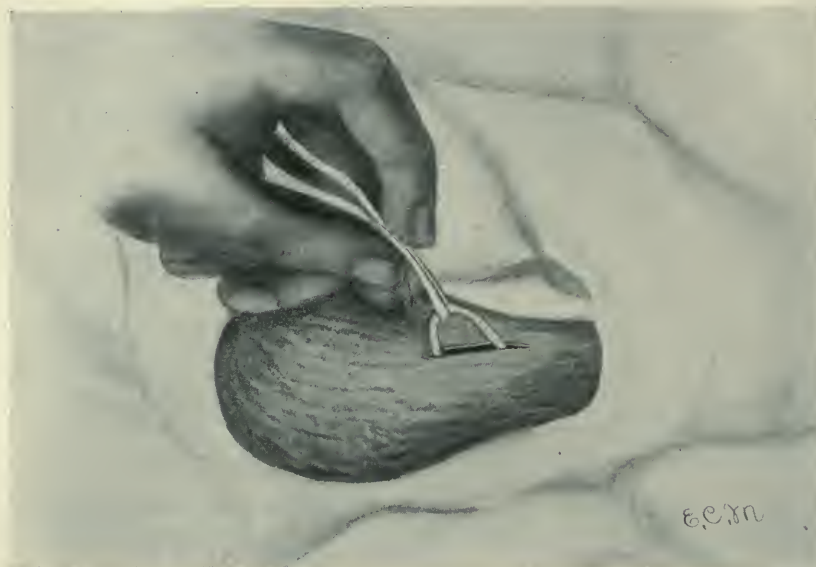


FIG. 1. VAS FREE AND ENTIRELY BARE FOR 1 INCH. TAPE RETRACTOR



FIG. 2. METHOD OF HOLDING VAS TAUT BY TAPE, AND OF HOLDING NEEDLE FOR INJECTION

If the exposure of the vas is properly done no injury to other cord structures will occur, and no hemorrhage. With a piece of tape or gauze under the vas for traction and elevation, it may be held taut, facilitating insertion of the needle (see fig. 2). A hypodermic needle with a short point, containing a horsehair or a strand of silkworm gut, is inserted into the vas, proof of it entering lumen being obtained by passing the obturator backwards and forwards. The naked vas is transparent enough to allow visibility of the horsehair or gut strand.

By supporting the needle and the retracting gauze, in one hand, between thumb and forefinger, it is easy to inject the fluid (see fig. 2). A Luer syringe, of 10 or 20 cc. capacity is ideal for this injection.

Dr. Belfield injects methylene blue on one side and eosin on the other, having the patient void after each injection of a colored solution, to insure patency of the vasa. This necessitates exposure of both vasa before injection, in a bilateral puncture. We do not feel that it is necessary to use these color tests. After proving the needle in the vas, a little sterile water may be injected; if it passes readily, the vas is open; if not, either the vas lumen is not freely patent, or the needle is buried in the vas wall. Rotation of the needle and reinsertion of horsehair or the gut strand, will right matters, and the sterile water may be tried again.

When the water enters readily, the medicinal solution may be used. Our practice is to force in the first 4 or 5 cc. rapidly on the theory that the sphincter of the ejaculatory duct is soon overcome, and it is well to force the solution into the vesicle before the sphincteric action is lost. Twenty cubic centimeters of the solution are put into each vas, and is followed by a little water, during the passage of which the needle is withdrawn.

The patient during the injection, experiences, one of two, or both sensations, the desire to void, with seepage of the solution injected, at the urethral meatus, or the sensation of the bladder filling up. We have no way of judging the amount of solution which passes directly into the bladder without first coursing through the seminal vesicles.

We are not in a position to state definite conclusions from vesiculograms; irregularities of outline are almost constantly found, with incomplete filling of one or both vesicles, dilatation of the ampullae, and various deviations from an equality of the two sides. Marked differences between the shadows of the two vesicles of a patient would seem to indicate pathology on one side at least; checking these differences with palpable findings of the vesicles, we hope in time to be able to recognize the radiographic evidences of pathology. Judging by plates alone it is not easy to state which vesicle is more diseased.

It should be stated that in one or two normal cases, having vasa injected as an incidental examination to scrotal operations, the shadows of the two vesicles were quite symmetrical.

If vesiculograms are desired, we have the patient empty the bladder, a large part of the opaque solution having accumulated therein, and with air injection, the exposures are made. We inject air through an ordinary soft catheter, with the bulb of a cautery apparatus. To insure the visualization of the vasa for any considerable distance, and a certain filling of the ampullae, the exposures must be made during the injection. For this procedure, we inject the two sides simultaneously. Herewith are shown reproductions, of some of the better vesiculograms made from the cases included in this report. We call attention to the difference between plates made with air injection, and those without.

When it is desired to inject the vas more than one time, a thin trough is made for the exposed vas, by inlaying into the scrotal incision, as a permanent retractor, a strip of rubber dam, half an inch wide. The wound is left open with the two ends of the rubber dam strip left outside in the dressing. Careful daily dressing is necessary to avoid infection.

Injections may be made every day or every other day for a week, after which the rubber dam should be removed, the wound cleansed, and the vas placed as deeply as possible. The wound is allowed to heal by granulation. This repeating of injection we have reserved for obstinate cases of gonorrheal arthritis only.

After having performed vas puncture in more than 50 cases, and upon both vasa in the majority of these, over a period of six months, we feel that we may make some definite statements as to the value of the operation. Alone, as treatment for vasitis and vesiculitis, it is not sufficient; it must be combined with the standard methods of treatment. Vas puncture does not promise a certain cure; in more than 50 per cent of our cases however, it has rendered the patients symptom-free, and during periods ranging from one to six months these patients have had no evidence of recurrence.

It must be remembered that the diseased prostate and vesicle is not always productive of the gonococcus, in ordinary smears, following massage. We believe with Gilbert Smith, that more than three or four pus cells to a high power field is indicative of disease. Finding pus, and knowing the history as one of chronic gonorrhea, one is justified in making the diagnosis of latent or active focal infection. Again, it is not correct to assume that only one vesicle is involved, because the other is not palpable.

As for choice of solution for injection in vas puncture; heretofore as far as we know, silver salts have been used exclusively. We have used collargol, in 5 and 10 per cent solution strengths, in most cases, but principally because we desired to obtain an adequate series of vesiculograms. We believe Mercurochrome 220 may give even better results, as we have obtained excellent results with this new solution in its use elsewhere in the genito-urinary tract. Mercurochrome 220 was used in a few of the cases reported here. The use of Cargentos, 20 per cent solution has also proved efficacious.

The principal objection raised to vas puncture, is, that one flushing of vas and vesicle is insufficient to rid these structures of a deepseated disease. This objection seems a sound one, but remembering the distinct difference, histologically, between the inner surfaces of the vas and vesicle, and that of the urethra, and that in the latter are numerous glands for hidden infection; also that the seminal vesicle is simply a series of diverticular-like pockets, all easily reached by injected solutions unless obstructed, we may rightfully assume that the solution bathes the entire

surface inside the vesicle, and remains for some time, even up to a period of weeks or months. This, we have proven in several instances. The urine of a man who has had vas puncture, is tinged for days with the injected solution, and secretions obtained from massage of vesicles and prostate, contain the medication for weeks, and in one case for four months after operation.

Complications and unfavorable results of vas puncture, may be summed up as follows:

1. Local infection in scrotum; this is very rare.
2. Hemorrhage from the incision, also rare, but always feared in the scrotum.
3. Leakage of injected solution, either near site of injection, or along vas higher up in cord; this occurred in one case, with prolonged induration along cord persisting for several weeks.
4. Invagination of skin at incision, and adhesion between skin and cord. This complication may result in bitter complaint on part of patient, either from real or imaginary cause; neuralgia of spermatic nerve, or unsightliness.
5. Epididymitis.

Results of vas puncture if ideal, are as follows:

1. Immediate passage of urine tinged with injected solution.
2. Vesiculogram proof of complete injection.
3. Prompt closure of wound, and rapid disappearance of induration in cord at site of wound and injection.
4. Cessation of urethral discharge, and all urethral symptoms.
5. Finding of, or evidence of spermatozoa, proving that there has been no occlusion of vas.
6. Disappearance of symptoms resultant from focal infection, as of arthritis.

When results are not satisfactory, we look for additional foci of infection, which may or may not have existed prior to vas puncture. Particular importance is paid to examinations for trigonitis, involvement of the sinus pularis, of Cowper's glands, and of the urethral mucosa. Of course there is always the possibility that insufficient treatment has been given the vesicle known to be diseased.

Following is a brief report of 55 cases which have had vas puncture at Walter Reed United States Army General Hospital, between the months of January and August, 1920. A few of the more striking results will be noted, and particular attention paid to end-results, so far as we have been able to determine them from observations over this period of seven months.

Classification of cases:

Class 1. Cases returned to duty within three weeks of the time of operation, apparently cured.

Class 2. Cases requiring additional treatment of urethra and prostate for periods up to six weeks.

Class 3. Cases with complications.

Class 4. Cases of gonorrheal arthritis.

Class 1: 40 cases

Of these 40 men only one returned after discharge from hospital; he had an acute urethritis, admittedly the result of new exposure.

Class 2: 15 cases

Of these many had simply a retardation in healing of wound, or a persistence of a slight urethral discharge. Some continued to have organisms and pus in secretion of vesicles and prostate. All, with one or two exceptions, have been returned to duty within the time indicated above, six weeks. The other cases will be further reported below.

Class 3: 5 cases

Of these, two cases developed acute prostatic abscess following the operation; one case an acute unilateral epididymitis; one a pronounced invagination of the scrotal skin at point of incision on the left side, with adherence of cord structures to skin; one an extensive seepage of collargol, along the entire length of the cord, followed by painful persistent induration of the tissues overlying the inguinal canal, and fever for several days.

The cases developing prostatic abscess had prior to operation, extensive involvement of that gland, and rather recent profuse urethral discharge. The case which developed the acute epididymitis, had also recently had a recurrent acute urethritis.

Class 4: 5 cases

Of these, all except one were immediately improved; three were cured within one week; one has shown steady improvement ever since the operation. One case was not improved; later it was determined that his arthritis was not of gonorrheal origin. One case, referred to as having shown steady improvement, had been bed-ridden for more than a year, in spite of treatment of urethra, and prostate, use of vaccines, baking, and the use of orthopedic appliances. Both knees were extensively involved, radiograms showing permanent arthritic changes; there was almost complete loss of motion in knee joints.

Since vas puncture, late in June, 1920, this case has regained complete motion of both knee joints; the swelling has entirely subsided, and except for weakness, he is able to be up and walking; at the present time, August 1, 1920, he walks on crutches. It should be stated that on admission to this hospital after a year of treatment, he showed a very acute urethritis, involving the entire urethra, and that he had also extensive involvement of the prostate as well as of the vesicles. His urethritis was cured promptly with Mercurochrome 220, and massage of prostate was done over a period of six weeks, until the gland showed marked improvement, with secretion negative for gonococci. After vas puncture the wound was left open, and the vasa injected with collargol every other day for eight days.

CONCLUSIONS

1. Vas puncture is an operation simple enough to warrant its use in view of the fact that it does offer an effectual method for eradication of foci of infection in the seminal vesicles.

2. Chronic seminal vesiculitis, with or without chronic prostatitis, if untreated, is a source of constantly recurring urethritis, and epididymitis. As a means of approach, vas puncture furnishes the best and most rational procedure for treatment.

3. Preceding vas puncture, or in addition to it there should be used, all the standard methods of treatment for urethritis and prostatitis.

4. Vas puncture should not be done unless other treatment is controlling associated conditions upon which vesiculitis is dependent, namely urethritis and prostatitis.

5. Vas puncture may honestly be described to a patient as the best means available for cure of the condition for which it is indicated; while not a positive cure, it does improve every case and in a majority leaves nothing to be desired.

6. In five of the cases included in the series reported here, we were able to obtain specimens of semen or copious amounts of secretion following massage of prostate and vesicles; in all of these specimens, active spermatozoa were found in abundance. In the first case operated upon it is interesting to record that the man has gotten married and that his wife expects to be confined within a few months.



FIG. 3. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION
Note large size of left vesicle. No air in bladder



FIG. 4. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION
Bladder has been irrigated; contains no air



FIG. 5. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION
Rubber catheter in bladder preliminary to air injection



FIG. 6. SAME CASE AS IN FIGURE 5

Bladder partially filled with air. Note striking increase of contrasts



FIG. 7. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION
Bladder partially filled with air. Some of collargol solution remaining in bladder.



FIG. 8. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION

Bladder partially filled with air; large amount of collargol remaining in bladder.



FIG. 9. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION
Catheter lying in bladder which has been filled with air. Patient extremely fleshy.



FIG. 10. BOTH VESICLES INJECTED WITH COLLARGOL, 10 PER CENT SOLUTION
Bladder filled with air

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THE TREATMENT OF GONORRHEAL COMPLICATIONS BY THE COMBINATION OF ANTIGONOCOCCUS SERUM AND A TEMPERATURE-RAISING AGENT

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In 1914 I began, at the State Bacteriological Laboratory in Stockholm, the preparation of a polyvalent antigenococcus serum by means of intravenously immunizing goats with living gonococcus cultures. This serum gave a complement fixation, it agglutinated and showed further a distinct protective influence against gonococcus toxins in experiments with guinea-pigs. The serum was carefully tested clinically, especially at the Clinic for Syphilology of the Caroline Institute, but also, though to a considerably smaller extent, in other places.

The first 120 cases were published in 1916 in the special publication to Professor Finger of Vienna on the occasion of his sixtieth birthday.¹ The action, in these cases, on different gonorrheal processes was briefly as follows: in the case of the usual infection of the mucous membrane (of the urethra, the cervix, the excretory ducts of Bartholin's glands, the conjunctival sac, etc.), in short, in the so-called open gonorrhea, no decrease in the number of gonococci could be ascertained. As regards the gonorrheal complications (the closed gonorrhea) e.g. arthritis, epididymitis, prostatitis, diseases of the eyes and adnexes, infiltrations of the Bartholin glands and periurethral infiltrations, the course was, however, different. In most cases painful symptoms had after five or six hours, sometimes earlier, obviously decreased or completely disappeared. This improvement was

¹ Arch. f. Dermat. u. Syph., 1916, xxiii, 774. See further Sv. Läkarsällskapets Förländingar, 23/3, 1915, and Arch. f. Dermat. u. Syph., 1915. Berichtteil., cxxii, 433.

either temporary or it progressed, on repeated injections, more or less rapidly to a partial or complete cure. Only a few cases were quite refractory.

The trials gave the impression that the acting principle of the serum, at least for the greater part, *was an antitoxic one*. Only by a neutralization of the toxins deposited in the attacked tissues, is it possible to explain the improvement, which occurred so quickly, often quite astonishingly, but which, nevertheless, gave no fixed points whatever as to the issue of the case. On the contrary, disappointments were often the result. I will relate two cases of arthritis, where it might be said, that in both cases the start was very good, but where, in the following course, the serum proved to have had an exceedingly good influence in one case, whereas in the other it had been of no use.

Case I (Professor Almkvist). The patient, suffering from arthritis of both articulations of the jaw, had for a week such painful symptoms, that he had not been able to partake of anything but liquid food. Four hours and a half after the serum injection he was able to open his mouth normally without difficulty and to move the lower jaw laterally. All pain had vanished. The result was permanent.

Case II (Professor Jacobaeus). Patient suffering from a *serious* arthritis, of several weeks duration, of the articulations of one knee and foot. Five hours after the serum injection, a striking improvement was noticed. There was a diminution of spontaneous pain and tenderness to pressure as well as a considerable increase of the power of motion. But this effect was only temporary. Later the condition became worse. Three more injections resulted only in a temporary improvement.

Although the greatest caution must be observed before drawing positive conclusions regarding a new therapeutic agent, still it may be said, that my antigenococcus serum at that time (1916) was superior to the gonococcus vaccines. In the same way as in the treatment with the latter, there were several cases where the serum was not successful. But there were, on the other hand, many cases, where the effect was remarkably good, and in some cases the treatment with gonococcus vaccine had previously been tried in vain.

Since my first experiments, I have been working with a view of improving my serum, and by changing the technique of immunization, I have succeeded in getting it of a decidedly higher value. Of late, I have used rams instead of goats. For the past year and a half, taking into consideration the sensibility of the gonococci to warmth, I have made experiments by letting the antibodies of the serum act at the same time that the body temperature of the patient was being raised. The gonococci would then be attacked by two factors noxious to them; antibodies and heat. In doing this I have added to the serum a certain quantity of some temperature-raising agent, availed myself in particular of dead bacteria-cultures, e.g., of typhus bacilli. With this preparation, thus based upon the double principle: *action of antibodies-fever*, trials have been made in more than a hundred cases of different gonorrheal complications (particularly arthritis, epididymitis and prostatitis). The effect has in most cases proved to be simply superior. The most serious cases of fresh arthritis have after one or two injections gone to complete cure in an uncommonly short time (one to two weeks). For instance, one patient with arthritis of the feet and knees, had one day to be carried on a stretcher into the lecture hall, and a few days later was so well that he was able to walk. In many cases, where the gonococcus vaccine had had no effect at all (not even after some ten injections), a treatment with serum has been followed by an obvious improvement at once. In some few cases, neither a previous treatment with gonococcus vaccine nor a later treatment with serum has been of any use (secondary infection?). Most often cases of prostatitis have been cured in one week. The same rapid response was noted in epididymitis. A large gonorrheal cutaneous abscess in the perineal region healed after a single injection in one week.

The untoward effects of the serum treatment are chills and high fever after the injection, considerable tenderness at the site of injection (the gluteal muscles), persisting for some days, and at times a passing tenderness in the inguinal lymphatic glands.

THE VALUE OF PYELOGRAPHY IN THE DIAGNOSIS OF NEOPLASMS OF THE KIDNEY¹

J. A. C. COLSTON

The knowledge which the urologist obtains through pyelography has been of inestimable value in the correct diagnosis of obscure conditions of the kidney, and we are now able to obtain, thanks to this simple procedure and the experience gained from the interpretation of many plates, a clear understanding of abnormalities in the pelvis of the kidney and their underlying causative pathology. Surgical disease of the kidney, almost invariably sooner or later, leads to malformation of its pelvis either through direct involvement of the pelvis itself or by distortion of an otherwise normal pelvis. These changes can be readily studied and the results correctly interpreted if the technique has been satisfactorily carried out and if the observer has a clear understanding of the pathology of the kidney and a broad experience in the interpretation of pyelograms.

An exploratory operation on the kidney was formerly by no means a rarity in any clinic, but the progress in the diagnosis of renal conditions in recent years has permitted the surgeon such accurate knowledge of the disease with which he is to cope, that this operation should now have practically disappeared.

The reactions which may follow as a result of pyelography are only very rarely alarming owing to improvements in the medium to be injected and careful attention to the technique. More or less severe pain, practically identical with that observed in kidney colic, is however of fairly common occurrence, and indeed this reaction is frequently noticed after the introduction of the ureteral catheter when no substance has been injected into the pelvis. When a definite diagnosis can be made without

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resorting to pyelography—as, for example, by the demonstration of tubercle bacilli and pus cells in the specimen collected from one ureteral catheter—the patient should not be subjected to this procedure.

Nevertheless, there are many cases in which, unfortunately, a definite diagnosis cannot be made, and one must resort to pyelography for a clearer understanding of the condition. To determine definitely the cause of a renal hematuria is very often extremely difficult, and it is in cases of this type that pyelography is of the greatest value. The diagnosis of essential hematuria should never be made unless a careful pyelogram has demonstrated the presence of a normal pelvis and the proper steps have been taken to eliminate the possibility of stone, tuberculosis, etc. It should not be forgotten that renal hematuria is a symptom which may indicate the presence of a serious condition and a diagnosis of essential hematuria should not be made until the more serious causes of renal bleeding have been thoroughly and systematically eliminated.

Many writers have called attention to the value of pyelography in the diagnosis of hypernephroma, the most common variety of kidney neoplasm. The changes in the shape of the renal pelvis caused by the growth of these tumors are well-known and can be readily demonstrated by a good pyelogram. Similar changes, of course, are caused by the other rarer types of tumors and are also easily demonstrable. Three unusual types of kidney tumors have recently been observed in this clinic in all of which the diagnosis was assured by pyelography. The differentiation of the type of tumor before operation is of course impossible, as the diagnosis, from the point of view of the pyelogram, depends entirely on the distortion of the renal pelvis which eventually results from the extension of all types of kidney tumors.

The three cases reported below are excellent examples of the danger of an incomplete urological examination. These patients had been diagnosed as cases of essential hematuria. In one, fortunately, the tumor was of a relatively benign type and the patient has remained well, in the second case metastases were

found at operation and a fatal outcome resulted in a few months, while in the third case metastasis was demonstrable five weeks after the operation in spite of the fact that the tumor was apparently completely removed.

Case 1. A. C., age forty-two, complained of kidney colic and hematuria. The family history and past history were unimportant and the patient had had no serious illnesses. There was no history of gonorrhea or syphilis, and the patient had had no urinary symptoms prior to his present illness.

The present illness began two years ago when the patient had a severe attack of pain in the left flank radiating into the groin which lasted off and on, for three days. When the pain had disappeared, a large blood clot was passed in the urine. Since this time the urine has contained blood from time to time, and there have been four or five attacks of kidney colic, always on the left side. Following one of these attacks the patient states that he passed a small stone. For the past few months there has been an uneasy feeling in the left loin and back, with dull pain on exertion. The patient has lost no weight but states that he is losing strength. The last severe attack of pain occurred three days before admission, since which time he has passed large quantities of blood. The patient had had five cystoscopic examinations, but no definite diagnosis had been made, although one surgeon had advised that the kidney be removed.

The patient was a stout, well-nourished man with a quite evident anemia. General physical examination failed to reveal any abnormal findings. Neither kidney was palpable and there was no tenderness over the kidney regions, in the costo vertebral angles, or along the course of the ureters. The external genitalia were normal except for a slight retraction of the left testicle. The prostate was slightly broader than normal, but the lateral lobes were smooth, elastic and not indurated. The seminal vesicles were normal and no induration was noted at the base of the bladder.

The urine was bloody and microscopically contained a large number of red cells, an occasional white cell and a moderate number of epithelial cells.

Cystoscopic examination showed no residual urine. There was no intravesical enlargement of the lateral or median prostatic lobes. The trigone was somewhat hypertrophied and congested. The view was somewhat obscured by bleeding, which was seen to come in spurts from

the left ureteral orifice which was somewhat gaping and reddened, but there was no ulceration around it. The right ureteral orifice was normal in appearance. The bladder mucosa was everywhere smooth, and no abnormalities were noted. Ureteral catheters were easily introduced to each kidney. The specimen obtained from the right kidney was slightly blood-tinged and microscopically showed an occasional white cell and epithelial cell but no organisms. Phenolsulphonphthalein appeared, after intravenous injection, in four minutes, with an excretion of 25 per cent for a half hour. Only a few drops of blood were obtained from the left ureteral catheter. The transvesical specimen contained only a trace of phthalein.

The plain X-ray showed a slight enlargement of the left kidney, but the kidney shadows were not satisfactorily made out on account of the patient's thick abdominal wall.

A left pyelogram (fig. 1) was done and showed an incomplete filling of the pelvis. Some thorium had been forced into the lower calyx, but the upper and middle calyces were unfilled. The ureter was slightly dilated as it crossed the brim of the pelvis.

A diagnosis of tumor of the left kidney involving chiefly the upper pole, was made.

Operation: left nephrectomy, January 17, 1920. The kidney was exposed through an extraperitoneal incision in the loin, and at the upper pole a tumor was recognized. This latter was adherent to the diaphragm, but separated off fairly easily and it was evident that no extension of the growth had taken place. The kidney was removed in the usual manner, the pedicle being ligated with chromic catgut. The ureter was not obviously dilated and felt normal down to the brim of the pelvis. It was divided two inches below the kidney and the stump ligated. The wound was drained and closed in the usual manner. The patient left the table in good condition, having lost little blood during the course of the operation.

The specimen removed at operation consisted of a left kidney and about 2 inches of ureter. From the upper pole an irregular, nodular mass projected. This tumor was about the size of an English walnut and was covered everywhere by a smooth capsule of fibrous tissue. When the kidney was opened, it was found that the upper portion of the pelvis was occupied by a villous tumor which had apparently sprung from the wall of the upper calyx. The tumor had then grown upward, forcing its way above the upper pole of the kidney and the fibrous capsule, which was noted as covering the tumor, was then recognized as

the pelvis or wall of the upper calyx itself. The tumor had not invaded the kidney proper, the upper pole of which was somewhat atrophic. The lower pole was normal. The tumor consisted of a mass of villous processes arising from the wall of the pelvis. The latter was much thickened and in places there were areas of necrosis and infiltration.



FIG. 1. CASE 1. PYELOGRAM, LEFT KIDNEY

A small amount of thorium can be seen along the lower portion of the pelvis and in the lower calyx. No thorium has entered the upper and middle calyces. The kidney shadow cannot be made out on account of the patient's thick abdominal wall. The picture is somewhat blurred on account of the patient's respiratory movements.

Microscopically the tumor was found to consist of villous processes containing connective tissue covered with a single layer of flattened epithelial cells with large nuclei. The cells at the base of the tumor, in some sections, had definitely taken on malignant characters, and there was some invasion of the wall of the pelvis, but in no section had this

invasion reached the periphery. A diagnosis of malignant papilloma of the pelvis was made.

The patient made an uninterrupted recovery from the operation. In order to prevent, if possible, a recurrence of the tumor in the incision, he was given 1200 mgm. hours of radium, 100 mgm. being introduced in a capsule into the wound as soon as the drains were removed.

A letter was received from the patient nine months after operation, in which he stated that he was at work, had had no symptoms, had gained strength, and that the incision was well healed without sign of recurrence.

The case was a most instructive one, both from a clinical and from a pathological standpoint. The diagnosis of tumor of the kidney was suggested by the history of intermittent hematuria with attacks of kidney colic, with an X-ray plate which showed a slight enlargement of the kidney without any stone. The attacks of renal colic were, of course, interpreted as being due to the temporary occlusion of the ureter from time to time by blood clots. Cystoscopic examination proved that the source of bleeding was the left ureter, and the diagnosis was assured by the "filling defect" in the pyelogram and by the fact that no function was obtained from the left kidney. This latter finding is, however, difficult to explain when one studies the specimen removed at operation (plate 1). The kidney substance itself is quite normal aside from some pressure atrophy at the upper pole. It seems probable that, at the time of examination, the pelvis was so clogged with clots that no urine could find its way through to pass down into the ureter. The fact that no phthalein was found in the transvesical specimen would seem to eliminate the possibility of urine escaping down the ureter alongside of the catheter.

The true nature of the tumor was not recognized before operation. Israel made a correct preoperative diagnosis of papilloma of the pelvis of the kidney in a case which presented the symptom of intermittent hematonephrosis, and he states that this symptom should always suggest to the observer the probability of the presence of a papillary tumor of the pelvis. In our case, however, the kidney was not palpable and there was nothing in the history to suggest this important symptom.

The histological character of the tumor was very unusual in that the papillae were covered by a single layer of epithelial cells. Papillomata of the pelvis are commonly identical in structure with papillomata of the bladder, in which, of course, the villous processes are covered with varying numbers of layers of epithelial cells. Rarely, however, true papillomata of the bladder have been noted in which only a single layer of cells occurs, and such a case was recently observed in this clinic. We must assume, therefore, that the tumor under consideration is analogous to these rarer types of bladder papillomata.

Case 2. H. F., age twenty-one, complained of bloody urine. The family history and past history were unimportant. The patient had always enjoyed good health, had never been seriously sick, and there was no history of gonorrhea or luetic infection.

The present illness began with painless hematuria which was first noticed four months previously and was the first symptom noted. A thorough physical examination was made at this time by his physician and no abnormal findings reported. He was referred to a surgeon who made a cystoscopic examination and a ureteral catheterization. The bladder was quite normal but blood was found in the specimen from each ureter, from which the surgeon concluded that the bleeding was bilateral. X-ray examination was negative for stone, and neither kidney was enlarged. Two months after the onset of his hematuria, the patient's tonsils were removed in the belief that the condition was a glomerular nephritis. A month later the bleeding was more abundant than ever, and cystoscopic examination showed blood clots coming from the left ureter. The ureter was dilated at this time in the hope that this procedure would stop the hematuria. The urine at this time was reported to contain a great many epithelial cells. The patient had had several attacks of colic, usually on the left side, but had had one severe attack in which the pain was referred entirely to the right kidney.

The patient entered the Brady Clinic four months after the onset of his first symptom.

Physical examination revealed a fairly-well nourished young man, who had evidently lost some weight. The skin and mucous membranes were pale. No abnormal findings were noted in the head, neck or thorax. The left kidney was easily palpable and definitely enlarged.

It was slightly tender, but no irregularities or areas of induration could be made out. Examination of the abdomen failed to reveal any other masses.

The external genitalia were normal. There was a scar on the left side of the scrotum, the result of an operation for varicocele done six years before. There was no recurrence of the varicocele. The prostate and seminal vesicles were normal on rectal examination, and no induration was noted at the base of the bladder. The urine was bloody in three glasses, and microscopically contained many red cells, a few white cells, and numerous epithelial cells. No casts or organisms were found.

X-ray examination showed a marked enlargement of the left kidney with definite increase in the density of the shadow. Cystoscopic examination revealed a normal bladder. The ureteral orifices were normal, but blood was seen coming from the left ureteral orifice. The urine from the right ureteral orifice was clear. Catheters were easily introduced to each kidney.

The specimen obtained from the right kidney was clear and microscopically contained a few red cells and epithelial cells. No white cells or organisms were seen. The phthalein given intravenously appeared in three minutes and 20 per cent was excreted in a half-hour period.

The specimen from the left kidney was blood-stained and microscopically contained many red cells, a few white cells and numerous large epithelial cells with pale nuclei, which did not resemble the usual epithelial cells found in every ureteral catheter specimen. The phthalein appeared in five minutes and 10 per cent was excreted in a half-hour period.

A double pyelogram (fig. 2) was done and the plate showed a normal pelvis on the right side. The left pelvis showed a marked filling defect and only a small amount of thorium could be seen along the mesial border of the pelvis and in the upper calyx. The ureters were not dilated.

A diagnosis of tumor of the left kidney was made. It seemed probable that the tumor involved principally the lower portion of the kidney with destruction of about one-half or more of its secreting tissue, and had occupied almost the entire cavity of the pelvis.

At operation on March 26, 1920, Dr. Young exposed the kidney in the usual manner through an extraperitoneal incision in the loin. The kidney was found to be enlarged and the lower pole was irregular and nodular.

The kidney was freed from adhesions, which were most marked about the lower pole, and brought up into the wound after division and ligation of the ureter. The pedicle was then found to be shortened, thickened, and infiltrated, and along the aorta and closely adherent to it was felt a mass of glands which were certainly involved. In separating the



FIG. 2. CASE 2. DOUBLE PYELOGRAM

The right pelvis and ureter are normal. Only a thin streak of thorium has penetrated along the inner border of the pelvis of the left kidney and in the upper calyx, suggesting that the pelvis has been filled presumably by a tumor. The left ureter is not dilated.

peritoneum from the kidney, to which it was closely adherent, a small tear was made through the former. This tear was closed with a suture, but the tissue at this point was hard and friable, and the operator felt that there was definite extension of the tumor into the peritoneum. The glands along the aorta extended as far as its bifurcation, were densely

adherent, and in view of the involvement of the peritoneum already demonstrated and the probability of serious hemorrhage, an attempt to remove these glands was considered inadvisable. The kidney was then removed in the usual manner and a capsule containing 100 mgm. of radium was introduced over the involved glands and left in the wound for six hours. The patient left the table in good condition.

The specimen consisted of a markedly enlarged and nodular kidney, the tumor apparently occupying for the most part the lower pole. The pedicle was thickened and infiltrated, and at several points it was evident that malignant tissue had been cut through. On section (plate 2) it was seen that almost the whole kidney, save a small portion of normal tissue at the upper pole, had been destroyed by a glistening, whitish tumor which had also grown out into the pelvis, entirely filling its cavity, except for a small portion along its mesial border and part of the upper calyx.

Microscopically the tumor was found to consist of irregular masses of large cells with pale nuclei definitely epithelial in type. There were numerous mitotic figures. No definite arrangement of the cells could be made out, but in some areas the tumor cells closely resembled the cells of the secreting tubules. There was little fibrous tissue through the tumor and only an occasional area of necrosis was observed. A diagnosis of carcinoma simplex was made. It was considered that the tumor probably arose from the epithelium of the secreting tubules.

The post-operative course was uneventful and the patient left the hospital three weeks later. He was well for two months, when signs of involvement of the right knee and the lungs developed. He died three months after operation, evidently from pulmonary metastasis. No autopsy was obtained.

When the patient was first seen at this clinic, he presented the classical signs of pain, tumor and hematuria, so that there was strong presumptive evidence that a renal neoplasm was present. Cystoscopic examination determined the source of the bleeding to be the left ureter, and ureteral catheterization revealed that the function of the left kidney was markedly reduced. The diagnosis was made certain by the pyelogram.

The source of a renal hematuria can only be accurately determined during cystoscopic examination by actually observing blood issuing from the ureteral orifice. An attempt to draw

conclusions as to the source of the bleeding, from the specimens collected by ureteral catheters, often leads to an erroneous interpretation, as it is well known that the trauma of the introduction of the catheters invariably causes some hemorrhage, which may vary from a few red cells in the centrifugalized specimen, to a collection of almost pure blood. The latter event is quite commonly seen when the catheter has been introduced too high into the pelvis with resulting trauma to the tissue of the kidney.

Study of the drawing of the kidney (plate 2) shows that it had been almost entirely destroyed by the tumor, and it is surprising that the small amount of secreting tissue left should have been able to excrete 10 per cent of phenolsulphonphthalein.

The occurrence of a most malignant type of carcinoma, as the tumor proved to be on microscopic study, in a patient of such comparative youth, is certainly a most unusual observation. It was the general impression of those who observed the case before operation that the tumor would prove to be either a sarcoma or, more probably, a hypernephroma.

Case 3. W. K. P., age thirty, complained of pain in the left kidney and blood in the urine. His family and past history were irrelevant.

The patient first noticed blood in his urine seven months previously. At this time the bleeding came on without any known cause, was not associated with pain and lasted for about a week. Several periods of this painless hematuria then followed. About three months after the first appearance of the blood, the patient noticed pain in the left lumbar region and in the back. This persisted, with variation in intensity, until a month later a very severe attack occurred, the pain being located in the lower abdomen and kidney region. For the past three months similar attacks of severe pain have necessitated the administration of morphia. In the periods between these attacks, dull, aching pain has been continuously present and bleeding has occurred, apparently bearing no definite relation to the more severe attacks of pain. For the past month, the urine has been constantly bloody and the patient has lost strength. He has lately had some frequency, urgency and hesitancy.

Physical examination revealed a fairly well nourished young man, with an evident anemia. Examination of the head, neck and chest failed to reveal any abnormal features. The right kidney was not

palpable, and no tenderness was elicited over it or in the costo-vertebral angle. A definite mass was felt below the left costal margin, which moved freely on inspiration. This mass was smooth, freely movable, and quite tender. No nodules or irregularities could be made out over it, and the mass seemed definitely to be an enlarged kidney. The abdomen was otherwise quite normal except for a well healed appendectomy scar.

The external genitalia were normal except for a moderate left varicocele. The inguinal glands were not enlarged. On rectal examination the prostate and seminal vesicles were normal, and there was no induration at the base of the bladder.

The urine was bloody in three glasses and microscopically contained many red cells, a moderate number of white cells, and epithelial cells. No organisms were seen.

On cystoscopic examination, the prostatic orifice was normal. There was some congestion about the trigone. The right ureteral orifice was normal and clear urine could be seen coming from it. The left ureteral orifice was slightly gaping and blood-stained urine was observed coming from it in characteristic spurts, especially when pressure was made on the left kidney. The bladder mucosa was everywhere normal. Catheters were easily introduced to each kidney.

The specimen from the right kidney was clear and microscopically contained red cells and epithelial cells, and an occasional white cell. No organisms were found. Phenolsulphonphthalein (given intravenously) appeared in three minutes, and 35 per cent was excreted in a half hour.

The specimen from the left kidney was bloody and microscopically contained a large number of red cells and white cells, a few epithelial cells, but no organisms. Ten per cent phthalein was excreted in a half hour.

Ten cubic centimeters of 15 per cent thorium was injected by gravity into the left kidney and a beautiful pyelogram obtained (fig. 3). The upper calyx is normal and the minor calyces clearly outlined. The lower calyx is normal in outline, but is very evidently pushed up and gives one the impression that it has been rotated. The whole pelvis lies higher than normal and beneath it can be seen the shadow of a large tumor which extends to within an inch of the crest of the ilium. The ureter is not dilated.

A diagnosis of tumor involving the parenchyma of the left kidney was made.



FIG. 3. CASE 3. LEFT PYELOGRAM

The pelvis and calyces are quite normal in outline. The lower calyx gives one the impression of either being compressed upward or of being rotated. The whole pelvis is higher in position than normal. Below the pelvis can be seen a large rounded shadow extending to within an inch of the crest of the ilium. The operative specimen (fig. 6) showed this shadow to be caused by a large cyst filled with blood clots.

Operation, left nephrectomy, October 30, 1920. The usual extraperitoneal loin incision was made and on dividing the muscles a large, rounded, freely movable tumor was encountered which was continuous with the kidney. The latter was located high up beneath the costal margin but it was fairly easily freed of a few adhesions. The peritoneum was closely adherent to the surface of the tumor and there were numerous adhesions. The ureter was not dilated and was ligated and divided. The tumor was then removed and the kidney pedicle ligated in the usual manner. The wound was closed with drainage.

The post-operative course was uneventful and the patient left the hospital on the thirteenth day.

The specimen removed at operation consisted of the left kidney from the lower pole of which projected a smooth, globular tumor mass. The tumor was soft, without any areas of induration, and gave one the impression of a rather thickwalled cyst. It was apparently quite distinct from the pelvis. The specimen was hardened to preserve the contents of the cyst and section (plate 3) at a later date, showed that the upper pole of the kidney was quite normal in appearance. The tumor itself was seen to consist of a smooth walled cyst which was filled with blood clots. The cyst wall was formed by a thick fibrous membrane and the clots in direct apposition to this membrane, were evidently undergoing organization. The superior portion of the wall of the cyst was occupied by a papillary tumor which had extended into the wall but had apparently not invaded the kidney substance which covered the cyst at this point. This tumor was evidently the source of the hemorrhage.

Sections of the tumor for microscopic study showed it to consist of papillae covered with several layers of epithelial cells with a small amount of connective tissue framework. In some areas there was a typical adenomatous appearance. The tumor had invaded the cyst wall and here the cells were larger with no very definite arrangement, and numerous mitotic figures were seen. There was no invasion of the kidney tissue which was quite normal aside from the well-known changes due to pressure atrophy. Study of the cyst wall remote from the tumor showed it to consist of a fairly thick layer of fibrous tissue with adherent organizing blood clots. There was no epithelial lining to the cyst. A diagnosis of papillary adeno-carcinoma, probably arising from the epithelium of the secreting tubules, was made.

The patient returned for observation five weeks after operation. The wound was nicely healed, but in the left side of the neck four large

glands were felt, which were regarded to be in all probability metastatic in origin. He is at present under treatment with X-ray and radium emanation points have been introduced into the glands.

When seen at this clinic, this patient, too, presented the three classical signs of a kidney tumor, and the diagnosis was readily confirmed by the results of ureteral catheterization and especially by the pyelogram. The clear-cut pyelogram obtained, showing a pelvis completely filled, proved that the tumor was not invading the pelvis, and in all probability was confined to the renal parenchyma itself. This hypothesis was confirmed by the specimen. Although it is as yet too early to predict the ultimate result, the presence of enlarged cervical glands, which are presumably metastases, renders the prognosis extremely unfavorable. It is surprising that metastasis should have occurred so early, as the operative specimen looked very favorable for an ultimate cure and the tumor was completely removed with a wide margin.

The diagnosis of a kidney tumor must be made early, before the advent of the three classical symptoms, if the results obtained by operative treatment are to be at all satisfactory, and it is distinctly discouraging that hematuria had been a persistent feature in the three cases which have been presented for at least four months before these cases were seen. Only half-hearted attempts had been made to determine the true source of the bleeding, and the patients had been treated by palliative measures and reassurance. Unfortunately, the hemorrhage from a kidney tumor will lessen, or almost completely cease, under complete rest in bed, and the rapid improvement which occurs under these circumstances too often leads the physician to a wrong interpretation of the case, and to a delay which inevitably destroys whatever chance the patient may have had.

Pyelography is the one best measure which we possess for an early diagnosis of kidney tumors, and this procedure should be employed in every case in which the cause of hemorrhage from a kidney cannot otherwise be determined. Provided cystoscopic examination is undertaken at the time of the bleeding, the

affected side can almost invariably be determined by direct observation of the ureteral efflux. Idiopathic renal bleeding, the so-called essential hematuria, undoubtedly does occur, but such a diagnosis should never be made until a thorough study of the kidney by ureteral catheterization and pyelography has eliminated the possibility of more serious disease.

PLATE 1

Case 1. Specimen removed at operation. The papillary tumor can be seen filling the upper calyx. At the time that the pyelogram was done the entire pelvis was probably filled with blood clots which accounts for the fact that only a small amount of thorium is present along the lower border of the pelvis and in the lower calyx.



PLATE 2

Case 2. Specimen removed at operation. The tumor has destroyed the entire kidney save for a small portion of the upper pole, and has grown into and almost completely filled the pelvis. The pyelogram (fig. 2) can be readily understood by a study of this drawing.



PLATE 3

Case 3. Specimen removed at operation. The tumor can be seen at the upper portion of the cyst wall. The cyst itself is filled with blood, in all stages from fresh blood to organizing clots. The tumor has not invaded the kidney tissue nor has it involved the pelvis.



THE TESTES AND CERTAIN VASO-MOTOR REACTIONS OF THE PENIS

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EFFECTS OF CASTRATION

It has been noted in man that complete castration, if done before puberty, prevents further development of the seminal vesicles and of the prostate gland. This has been corroborated by experiments on lower animals. In certain animals, structural changes in the prostate seem to parallel changes in the testes (1). This relation of the testes to the prostate was pointed out by John Hunter in 1775 (2). Cowper's glands also atrophy after castration (3). However, the penis' growth, while inhibited, seems not necessarily annulled (4). The sexual impulse may persist, at least to some extent, in castrated animals (5). Changes occur in their mental character, although the intellectual capability is retained and important positions have been filled by eunuchs. Nares, a eunuch, is said to have been one of the ablest Roman generals (6). The breasts may enlarge from an increased fat production. Increased fat deposit also occurs in other localities. The hair fails to develop on the body and face, although it may be thick on the scalp. The voice preserves the soprano, or high pitched, tone of boyhood, at least until late, and the larynx resembles that of a child (7).

Changes in the growth of bones occur in castrated animals; thus certain bones of castrated rabbits become longer than the controls (8). In eunuchs, or in men with functionless testes, this also occurs; thus the eunuchs of Cairo can be distinguished in the crowd by their height (9). Eunuchs have an infantile

type of pelvis (Tandler and Gross) and castrated lambs have smaller, although roomier pelves, than non-castrated ones (10). In development, the individual takes on an infantile—not a female—type (11).

If the testes are removed from young stags the antlers do not develop or, if castration is done when the antlers are developing, they atrophy (12). In the case of cocks, castration arrests the development of the comb and wattles and causes skeletal changes (13), but contrary to the usual belief, Sellheim claims that the spurs even become somewhat longer. At the breeding season the male frog develops a thickened pad of skin on the first digit of the fore limbs and the muscles of the fore legs develop, but if castration is done, these changes do not occur. However, if a piece of testis is introduced into the dorsal lymph sac of a castrated frog, development occurs as normal (14). There is some question whether this is a central or a peripheral action (15). Stimulation of the *nervi erigentes* in normal adult dogs causes erection of the penis and ejaculation, while in castrated animals it causes merely slight congestion (16).

Castration affects certain organs which are not in direct relation to the sexual apparatus, i.e., the thyroid, thymus, pituitary (17), adrenal cortex, central nervous system, etc., and produces changes in metabolism (18).

TRANSPLANTATION EXPERIMENTS

In 1849, Berthold successfully transplanted testes into castrated cocks (19). These animals preserved their comb, wattles and other male characteristics. These results have been recently corroborated by Guthrie (20). Foges claims that castrated animals so treated showed certain differences from non-castrated ones (21). If a remnant of the testes is left at operation the animal may retain its normal characters and it is difficult to completely caponize cocks. These are the criticisms which can be urged against some of the earlier transplantation experiments.

The testicular tissue is easily injured by mechanical disturbances. The spermatogenic cells seem especially sensitive to

transplantation (22). In 33 rats on which transplantation was done by Castle and Phillips, 28 showed no signs of infection and in these "the epididymis was flabby, and in the region of the graft there was either a very small yellowish body or nothing but a bit of connective tissue surrounding the old stitches." "The microscopic examination was entirely negative so far as showing the presence of living testicular tissue."

In Göbell's experiments transplantation of the whole testis into guinea pigs failed, while transplantation of pieces were more successful (23).¹

Lydston and others report successful transplantation of testicular grafts in man (24). In Stanley and Kelker's recent operations on man, denuded testes were grafted on the atrophied gland of the recipient by Lydston's method. These individuals showed marked improvement and increase in general efficiency (25).

Steinach claims to have produced masculinization of female rats by transplanting testes into them (26). It has been shown that Oophorin, an ovarian preparation, acts intensely on the metabolism of the castrated male animal (27) and that extracts of bull testes influence the growth of bone in both male and female animals. C. E. Walker made preparations by aseptically pounding cock's testes in a mortar, adding normal salt solution, straining through muslin, but without using preservatives. Such preparations, when injected into two hens, produced an increase in size of the comb and wattles and when the injections were discontinued these shrank in size (28), in other words, such injections induced the development of certain male characteristics (29). However, it may be remembered that repeated subcutaneous injections of extracts of ergot into cocks, presumably by acting on the circulation of the comb, cause its hypertrophy (30). According to Loewy, feeding of testicular substance to capons caused an increase in the size of the comb and wattles (31), and prevented the usual skeletal changes, but he admits that his series was too small to permit of positive statements.

¹ No attempt is here made to give a complete bibliography of the subject, but to furnish only references corroborating the data given.

Dor, Maisonnave and Monziols report that in rabbits the subcutaneous injections of glycerine extracts of bull testes, prepared by d'Arsonval's method, inhibited the development of bone (32). In these experiments both male and female animals were used. Intravenous injection of glycerine extracts of dog, rabbit or guinea pig testes into dogs cause an increase in vesical capacity and of the contractility of the vesical neck and membranous urethra. Biedl says these vesical changes correspond to the genito-vesical reflex. Extract of bull testes gave no such results. The injections also caused an hypersecretion of the prostate and of Cowper's glands (33).

In George Walker's experiments, dogs were castrated, then injected with a testicular fluid, prepared by grinding dog testes and extracting with 50 per cent aqueous glycerine, straining through fine cloth after it had stood fifteen hours in the ice chest, finally adding tricresol to make one-fifth of 1 per cent. Castrated dogs treated with this preparation showed the same prostatic changes as untreated ones. However it must be noted that Walker's preparation contained tri-cresol and was allowed to stand for weeks in the room at ordinary temperature (34). Under such conditions a labile chemical compound could easily undergo change, although the solution remain sterile. Wheelon and Shipley showed that transplantation of testicular tissue relieved, to some extent, the vaso-motor depression, which resulted from castration (35).

The testes thus influence the development and maintenance of the secondary sexual characters; i.e., those characteristics found only in the male and not directly connected with the generative organs. However, according to Marshall the secondary sexual characters are not in all of the lower animals correlated with the essential organs of reproduction.

This influence must be due to some chemical compound formed by the testes. At one time, it was believed that the external testicular secretion was absorbed into the blood and thus exerted this action (36), but now the evidence is that these characteristics depend upon an internal secretion formed by the interstitial cells first described by Leydig (1850) and not upon

the cells of the spermatogenic tissue, as the latter atrophy after tying the vasa deferentia (37), while the interstitial cells remain apparently uninjured (38). Rams and cocks, after ligation and division of both vasa deferentia, develop normal male characteristics (39). In such animals, the sexual activity, after a short period becomes normal, although reproduction is impossible. Likewise, a study of men on whom ligation of the spermatic duct has been performed and of certain cryptorchids of lower animals, shows that those with normal interstitial tissue, but with degenerated semeniferous cells, possess normal male characteristics. In cryptorchid animals, which retain the male characteristics, the interstitial cells persist (40) while those cryptorchids, which act like castrated animals, have none (Mathieu). According to Bouin and Ancel (41) aqueous and glycerin extracts of ectopic testes, taken from various mammals and which were proved by the microscope to possess no seminiferous glands, when injected subcutaneously into castrated guinea pigs prevented the undue growth of bones, which occurs in castrated animals, and preserved the size of the penis and vesicules seminales.

Ontogenetically the interstitial tissue and the semeniferous glands are independent, the former developing first (Bouin and Ancel, p. 492). In old age the semeniferous cells degenerate, while the interstitial cells persist (p. 493) and the same relation holds in certain diseases (42). However, Ishibasi reports that he has found no relation between the proportions of the interstitial cells and the secondary sexual characters (43).

The part which the cells of Sertoli may play in this process is unsettled (44). Wheelon quotes Tournade to the effect that long continued ligation of the vasa deferentia causes disappearance of the cells of Sertoli (45) and this was the experience of Bouin and Ancel. It may be noted that three cryptorchid pigs, studied by Bouin and Ancel, in which the testes were rudimentary and in which the cells of Sertoli were absent, were typical males with well developed genital tracts. It is claimed by some that morphologically the interstitial cells are not originally distinct from these cells and that certain insects, with well marked sexual characters, have no interstitial cells (46). As

Sertoli's cells do not increase in cryptorchid animals, it seems unlikely that they would play any direct part in influencing such characters. Retterer's work would suggest that these cells are derived from the epithelium of the seminiferous tubules (47).

EFFECTS OF INJECTION OF TESTICULAR EXTRACTS

In 1889, Brown-Séquard, then a man seventy-two years of age, reported that the subcutaneous injection into himself of a liquid, which had been filtered through paper, or through a Pasteur filter, and which was made from crushed fresh testes of dogs and of guinea pigs caused a feeling of rejuvenation and increased ability for intellectual work so that he was enabled to do work as he had not done for years. His spinal reflexes, (defecation) seemed more active. Dynamometric measurements made on him showed an increase in strength. These injections caused pain, etc., which often lasted several hours (48). Later d'Arsonval and Brown-Séquard prepared glycerine extracts of bull testes. These extracts (49) were filtered through a Pasteur filter, under pressure with CO_2 (50) and in some cases CO_2 under pressure was used to sterilize the preparation. Brown-Séquard's results were confirmed clinically by Variot (51) and the reports of certain other clinicians were favorable. Good results were claimed for its rectal use (52).

No doubt, as with other new therapeutic agents, its value was over-estimated (53) and negative results were soon reported. At present, this method is seldom used (54). Perhaps differences in the reports were partly due to differences in the character of the preparations used. In some cases, glycerin was used as a solvent and this might play a part in such injections, but the question whether glycerin has any nutritive action has not been settled. However, it is well to remember that "Fresh unboiled extracts of various organs and tissues of the body have a distinct stimulating effect when administered subcutaneously to dogs, cats and other laboratory animals" (55).

Zoth and Pregl claimed that the injections of glycerin extracts of testes alone did not increase the functional activity of the muscles, but that daily exercise with such injections increased

it and that there was a greater increase than after muscle exercise alone. However, there is a possibility of suggestion in this method. Controls with glycerin were made (56). Increase in muscular force was also claimed by Capriati (57). However, one would not expect a direct action on the neuro-muscular apparatus from testicular extracts, because castrated animals are not less strong than controls. One might expect a central action. In old age testicular changes are only one factor in general tissue change.²

Attempts were made to isolate the compound which was believed to produce this dynamogenetic action. Poehl isolated from testes, as well as from other organs, a base Spermin ($C_5H_{14}N_2$) (58) which was probably identical with the base discovered by Schreiner in semen. This, Poehl believed to be the active agent in Brown-Séguard's preparation, but Brown-Séguard denied this (59) and Dixon found that Spermin had little to do with the physiological action of testicular extracts (60).

Graefenberg and Thies claim that rabbits are very sensitive to the intravenous injection of testicular emulsion. After its injection, they become restless, develop incoördinate movements and fall on their side with convulsions. Usually punctiform hemorrhages were found in the pleurae. The heart and blood vessels contained no thrombi. Rabbit testes are claimed to be more toxic to them than those of other animals used. In the case of guinea pigs, a different species, the testes were not toxic, at least in small amounts (61). The symptoms produced by the intravenous injection of such emulsions are similar to those resulting from the intravenous injections of peptones or of so-called ferments (62).

Dixon used testes of freshly killed animals, mainly rats and guinea pigs. These testes were macerated with normal salt solution; strained through muslin and filtered through filter paper. Intravenous injection of this solution into cats produced an immediate slight fall in the systemic blood pressure, which Dixon believed to be cardiac in origin. This was followed by a

² Féré claims that Mattei antedated Brown-Séguard in proposing the use of testicular extracts. See Mattei. *De la résorption de la liqueur seminale, de son action tonique excitante sur l'homme et sur la femme.* Paris, 1878.

second fall, which was associated with cardiac inhibition. Both falls are eliminated by atropin, at least when small amounts of the extract are used. Boiled extracts do not produce this second fall. Subsequent injections produced a diminished effect. Intravascular clotting was not seen. In dogs, only a single slight fall was produced. This was associated with cardiac inhibition. In goats, relatively small injections produced an initial rise, then a return to normal, which was followed by a second more marked rise. (63) The depression in the case of cats was associated with auricular depression.

According to Dixon, in dogs, testicular injections produce a marked dilatation of the intestinal vessels, without constriction. In goats, the first rise in blood pressure is associated with splanchnic dilatation and is cardiac in origin, while the second rise is associated with vaso-constriction. Ultimately, the splanchnic vessels dilate and produce a fall in blood pressure. In cats, there is a brief initial dilatation of the intestinal vessels which precedes the fall in blood pressure and if the cardiac inhibition is slight and respiration is not disturbed, there follows an increased dilatation. Large injections cause constriction after the initial dilatation, later a dilatation. The kidneys diminish in volume with even slight fall in blood pressure and after large injections this constriction may last even ten minutes, finally giving way to dilatation. The spleen responds like the intestinal vessels. Dilatation of the splanchnic area occurs even after atropin, which eliminates the fall in blood pressure due to small amounts of testicular substance. The hind limb shows a primary dilatation beginning just after the fall in blood pressure. This increase in volume is short. Boiled extracts produce dilatation of the intestines, limb and testes.

The dog testes, after an initial constriction, show a marked dilatation after testicular injections. This dilatation is apt to be prolonged and to occur in a series of waves, but in goats, the testes constrict (64).³

³ Dixon noted that epinephrin in amounts which raised the systemic blood pressure dilated the testes, while the pressure was high; that amyl nitrite causes a passive shrinking in testicular volume, that cantharides, which produced a marked fall in blood pressure, constricted the testes and kidneys, but dilated the splanchnic area and that caffein dilated the testes.

Injections of extracts of epididymis caused a very marked and immediate dilatation of the splanchnic and testicular vessels, somewhat different from the extract of the whole gland. By mouth, testicular extract produced a fall in blood pressure, like the intravenous injection of boiled extract.

Precipitation with a few drops of 10 per cent acetic acid threw out a nucleo-proteid, which, dissolved with 1 per cent Na_2CO_3 and injected, produced after a latent period, a fall in blood pressure and slowing of the heart. The spleen, limbs and testes dilated, while the kidneys contracted. In some animals it produced leucopenia. The neutralized filtrate after removing the nucleo-proteid acted like a boiled extract. Salvioli reports a delay in coagulation from testicular injections, but Loewy would explain this as associated with the blood changes, as there is first an hypo- then a hyperleucocytosis.

As yet we have no reports as to the action of extracts made from testes in which there is little or no semeniferous tissue (cryptorchids).

CHEMISTRY OF THE TESTES

The mammalian testes have been studied chemically, at least to some extent. According to Gerhartz, bull testes contain 87.4 per cent water (65) and in the case of rams, Dixon estimated it to contain 87 per cent. The testes of rams contain no albumoses or peptones (Dixon) although Pick claims both to be present in bull testes (66). Leucin and tyrosin, which have been found, are believed by Halliburton to be of post-mortem origin (67). Cholin is a normal constituent of bull testes (68), but was not found in those of rams (Dixon). Arginin, (69) hypoxanthin, xanthin, thymin, and lysin have been found as autolytic products (70). R-lactic acid is claimed to be an autolytic product (71). Various enzymes are also claimed to be present (72). Adenin was not found by Schindler (73), but Levene finds it in the testes of fishes. He also found guanin, thymin and cytosin (74).

According to Koch and Woods, the testes in the cases of the very young contained 2.78 per cent total lecithans, of which 1.43 per cent was kephalin and the remaining 1.35

per cent was lecithin. In the aged, the total lecithans was 2.2 per cent. Of these 1.2 per cent was kephalin and 1 per cent lecithin (75), i.e., young testes contain proportionally more lecithin than those of the old. Glycogen (76), creatin, inosit and cholesterin are claimed to be present (77), but glycogen may be present only at certain periods (Treskin).

From the testes of fishes, Miescher obtained compounds which he called protamines (78). These protamines occur bound to a nucleic acid. The protamines have been studied by Kossel and his pupils. Salts of protamines when injected into the circulation cause a marked fall in blood pressure in atropinized dogs. The blood pressure remained low for twenty-five minutes. Protamines delay coagulation (79).

The testes of cryptorchid animals, i.e., animals whose testes contain no spermatogenic tissue, convert starch into glucose. This action Hervieux attributes to a diastatic ferment (80). Cryptorchid testes show a marked increase in neutral fats. This increase is especially marked in the cells of Sertoli. The lecithans, or phosphorized fats, are increased in such testes (81).

Information as to the chemical nature of the internal secretion of the testes seems urgently demanded, not only because it seems to fill the clinical demands for a tonic, but mainly because it is one of the compounds selected by nature for a definite purpose (specific therapeutics). The external secretion of the testes has been considered a sovereign remedy for internal therapeutics by primitive people and even by more advanced races (82). Ellis suggests that some of this usage may have arisen from the ancient belief that this secretion is derived from the spinal cord.

If the testes are directly connected with both primary and secondary sexual characters then the effects of testicular extracts on the vascularity of the penis might perhaps be used as a biological test for studying the active constituents of this physiological aphrodisiac. This seemed especially hopeful when it was remembered that from very ancient times testes of animals have been taken by man as an aphrodisiac (83). In Stanley and Kelker's cases, and also in cases reported by other surgeons, transplantation of the testes was followed by erections and

sexual excitement, while Bouin and Ancel report that the injection of extract of interstitial tissue influences spermatogenesis. However, it is not yet proved that the aphrodisiac action of the testes is due to the compound which influences the secondary sexual characters and erection of the penis is only one feature of an aphrodisiac action.

PRESENT WORK

The dog penis is especially suited for this study as it is normally rigid, owing to the presence of an os penis. In our work we used sexually mature dogs as it seemed that very young ones did not respond. As oncometers we used glass tubes much like those described by Dale and Richards with a piece of Penrose rubber drainage tubing as a cuff. The foreskin was freed by a ventral incision and the penis inserted into a thin rubber condom the edges of which were then tied, together with the Penrose tubing, over the expanded rim of the glass oncometer. In some cases vaselin absorbent cotton was used as packing and the skin was brought together with stitches over the oncometer, which was then held rigid by means of a clamp at a slight angle to the normal line of the penis. The oncometer for the fore leg was made from a broken Salvarsan tube. The leg was inserted in a rubber Breeder's Bag, and this with a rubber collar, as in the case of the penis, was reflected over the tube and there held rigid by thick rubber bands and by ligatures. When the hind leg was used, the leg above the first joint was inserted into the oncometer. When the fore leg was used most of it could be inserted into the tube.

These oncometers were connected with glass U-tubes about 17 cm. high having an internal diameter of about 6 mm. In these, we used di-acetic ether as its specific gravity is higher than that of water, i.e., 1.03, hence will support the float better. As recording apparatus we used small corks carrying very fine aluminium tubing (no. 30 American). This tubing was bent so as to write against the smoked drum. The blood pressure was recorded from the femoral artery and injections were made into a femoral vein. The dogs were anesthetized with morphine and ether.

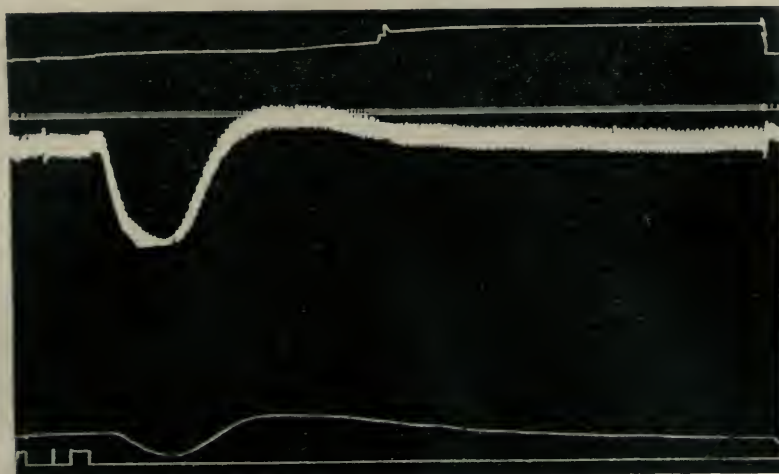
It seemed that we cleaned our arterial cannula more often than usual after the injection of extracts of undried testes (84). Testes and other tissues induce coagulation (85).

We started out with the idea that there were probably several depressor, or vaso-dilator substances, one or more of which were common to most organ extracts (86), and one of which acted mainly on the vessels of the penis. In this connection it is interesting to note that Dixon says that testicular substance contains two depressor compounds, one soluble and the other insoluble in alcohol (87). It might be expected that any agent which caused marked peripheral dilatation would cause some dilatation of the penis.

At first we used the expressed juice of bull testes diluted with water and preserved in the ice chest with chloroform, but only once did we get marked dilatation of the penis although it dilated the fore leg. Later dogs' testes were removed, dropped intact into chloroform and water, or into toluol, preserved in the ice box until used for this work. An extract was made from one and the other was used as a control. The control preparation was made by squeezing the cut-up testis through two or more layers of coarse cheese cloth, then adding NaCl 0.9 per cent or distilled water, and again filtering through cheese cloth, but not through paper. The preparations were made just before using as fresh testicular extract will only keep a few hours at ordinary room temperature (Dixon).

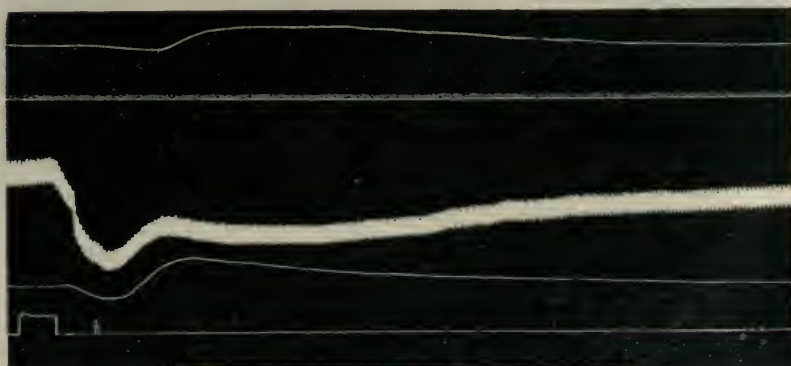
Such emulsions of dog testes usually caused dilatation of the dog penis. This dilatation of the penis occurred even without much dilatation of the fore leg, although the dilatation of the hind leg seemed more marked than in case of the fore leg. The penis dilatation usually comes on after the systemic blood pressure has returned to normal and the vaso-dilatation of the limb is subsiding (curve I). However, if the testes were kept too long they became inactive, at least did not dilate the penis, although they lowered the blood pressure. This would suggest that the chemical compound, which physiologically dilates the penis, is distinct from the other depressor substances of the testes. This view is supported by the fact that penis dilatation often comes on

after the blood pressure has returned to normal and the transitory vaso-motor changes in the hind- and fore-limbs are sub-



CURVE I. DOG (27 KILOS). INTRAVENOUS INJECTION OF AN EMULSION OF DOG TESTES (15 GRAM)

Top line penis volume. Hind leg record just above base line

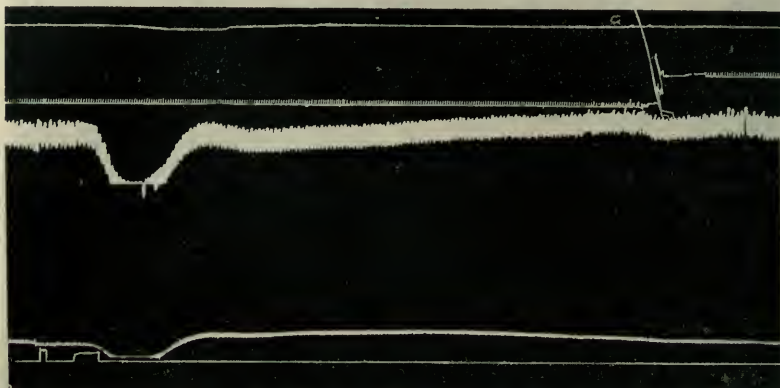


CURVE II. DOG TESTIS (14.7 GRAM) INJECTED INTRAVENOUSLY AS EMULSION FILTERED THROUGH CHEESE CLOTH

Lower line hind leg volume. Dog (18.5 kilos)

siding. In some cases emulsions of dog testes cause a more persistent fall in blood pressure with simultaneous rise in the volume of the penis and hind leg (curve II).

An emulsion of one dog testis (14.4 gram) was shaken for about five minutes with ether (U. S. P.) in a separatory funnel, then placed in vacuo at room temperature to remove most of the attached ether. However, it retained a slight odor of ether. The emulsion after this treatment was filtered through coarse cheese cloth. When injected intravenously it caused a fall in blood pressure followed by a slight rise, but produced slight, if any, dilatation of the penis. An emulsion of its control testis (15 grams) produced marked enlargement of the penis with slight initial constriction, then a transitory dilatation of the hind leg



CURVE III. DOG (27 KILOS). INTRAVENOUS INJECTION OF EMULSION OF FRESH DOG TESTIS (14.4 GRAM) SHAKEN ABOUT FIVE MINUTES WITH ETHER

Top line records penis volume. Lower line records volume of hind leg

and marked transitory fall in blood pressure. The evaporated ether extract produced no effect. In a second case, where the ether stood in contact with the emulsion for about one hour no effect was produced on penis volume or on blood pressure. This would suggest that ether precipitated, or in some way rendered inactive, the specific vaso-dilator substance of the testes and that the fall in blood pressure was not due to attached ether (curve III).

The testes of the adult dogs used by us weighed from 10 to 15 grams. We made no determinations of the amount of water they contained, but Dixon states that 87 per cent of the ram's

testis consists of water. On this basis a fresh dog testis weighing 13 grams would contain about 1.7 grams dry substance. One gram of commercial Orchic substance was extracted with water (9 cc.) and the extract filtered through filter paper. This solution caused a transitory, but marked fall in blood pressure, a slight enlargement of the hind leg, and a marked enlargement of the penis. The enlargement of the penis came on as the volume of the leg subsided (curves IV and V). An aqueous extract of Orchic substance (3 grams), filtered through paper, dilated the penis and caused marked fall in the blood pressure. The fore leg seemed only slightly affected.

The subcutaneous injection of a similar extract of Orchic substance (3 grams) produced, after a few minutes, slight dilatation of the hind leg and of the penis.

A 0.1 per cent acetic acid extract of 3 grams of Orchic substance, which was heated on the water-bath to remove coagulable proteins, caused a marked enlargement of the penis with fall in blood pressure, while control injection of 0.1 per cent acetic acid caused no effect.

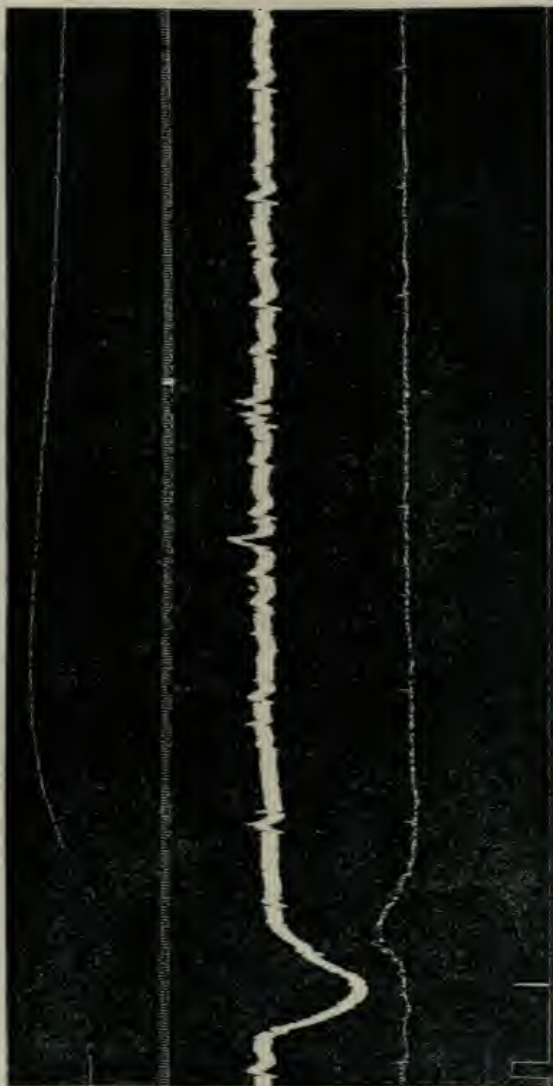
Orchic substance was shaken in a corked centrifugalizing tube with absolute ethyl alcohol, centrifugalized, the alcohol precipitated in such tubes with absolute ether and then again centrifugalized. This gave a white precipitate which in one dog caused constriction of the penis and some rise in blood pressure. However, in a second dog a similar preparation produced slight, if any, constriction and in a third dog it caused no rise. In a fourth dog it produced no effect on penis volume or blood pressure. The aqueous extract of the Orchic substance after this extraction with absolute alcohol gave a very marked fall in blood pressure and a well marked dilatation of the penis.

Even after cold extraction with ether (U. S. P.) the aqueous extract of dried Orchic substance gave a marked fall in blood pressure and dilatation of the penis. This is a different condition from shaking an emulsion of the fresh dog testes with ether, because, no doubt, in drying changes occur in the physical condition of the colloids with which presumably the specific vasodilator is physically associated.



CURVE IV. Dog (18.5 Kilos). MORPHINE SULPHATE 30 MGM. SUBCUTANEOUSLY

Ether—aqueous extract (9 cc.) 1 gram Orchic substance. Lower curve is made from left hind leg. Upper curve from penis. Second elevation on base here represents NaCl injection.



CURVE V. Dog (18.5 KILOS). INTRAVENOUS INJECTION OF FILTERED AQUEOUS EXTRACT OF ORCHIC SUBSTANCE (3 GRAMS)

Bottom line is base or zero line; line above is record from left fore leg; above is blood pressure record taken from the femoral artery. Above this seconds are recorded. The top line records changes in penis volume. Injection made at 2.15 p.m. Volume of penis returned to normal in about ten minutes.

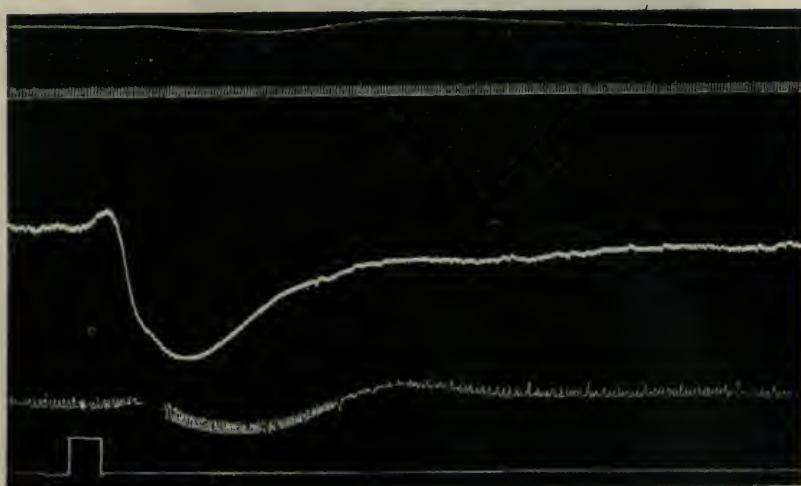
A filtered aqueous extract of Orchic substance (5 grams) was precipitated with a saturated aqueous solution of HgCl_2 . This precipitate was decomposed with H_2S , evaporated on the water bath under CO_2 , then extracted with absolute ethyl alcohol in a desiccator. The filtered alcohol gave a precipitate with absolute ether (88). This precipitate stood in contact with alcohol and ether three days. It produced a fall in blood pressure with well marked enlargement of the fore leg and a slight dilatation of the penis. Picric acid gave a precipitate from H_2O , which redissolved by means of a trace of NaOH , produced the same effects as the original solution, save that the penis dilatation and fall in blood pressure were less marked.

EFFECT OF OTHER TISSUE EXTRACTS

As testicular extracts cause vaso-dilatation of the penis it seemed desirable to compare its action with that of extracts of other organs. A filtered aqueous extract of dried corpus luteum (about 3 grams) taken from sows caused a marked persistent fall in blood pressure—a rise in volume of the fore-leg after an initial constriction and very slight dilatation of the penis (curve VI). A similar injection made from dried parotid gland of the ox caused a marked fall in blood pressure, a fall, then rise in volume of fore leg and a fair increase in penis volume. A similar extract of dried spleen of the calf caused a fall, then a rise in blood pressure, a marked temporary increase in volume of the fore leg and a fair increase in penis volume (curve VII). An extract made from dried spinal cord of the ox caused a marked persistent fall in blood pressure with increase in volume of the fore leg and penis. There seemed to be general peripheral vaso-dilatation (curve VIII).

According to Osborne and Vincent, fresh normal salt extracts of brain, spinal cord and sciatic nerves produce a transitory fall in blood pressure, and dilatation of arterioles in general, even after atropin. The intestinal vessels dilate at once, while the limbs dilate later. The circulatory depressor in the gray matter

of the brain is soluble in alcohol and ether and is not precipitated by phosphotungstic acid.⁴



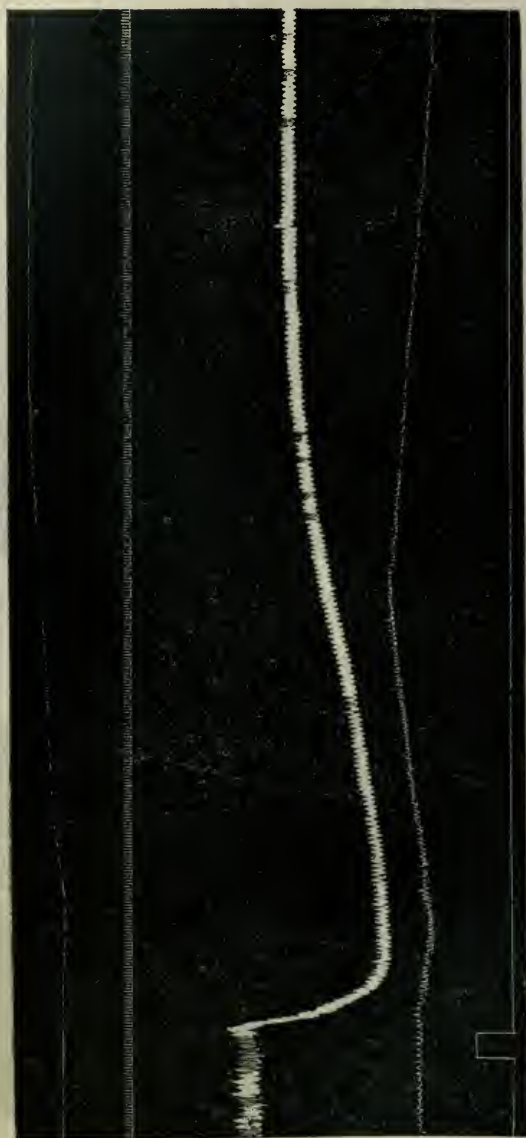
CURVE VI. DOG (12 KILOS). FILTERED AQUEOUS EXTRACT OF ABOUT 3 GRAMS
CORPUS LUTEUM (SOW)

Fore leg volume recorded as line above base line



CURVE VII. DOG (12 KILOS). INTRAVENOUS INJECTION OF AN AQUEOUS EX-
TRACT (FILTERED) OF ARMOUR'S DRIED SPLEEN OF CALF (ABOUT 2 GRAMS)

⁴ The dried preparations used were those marketed by Armour and Company.



CURVE VIII. Dog (12 Kilos). INJECTION INTRAVENOUSLY OF FILTERED AQUEOUS EXTRACT OF ARMOUR'S
DRIED SPINAL CORD, OX

EFFECTS OF VARIOUS DRUGS ON PENIS VOLUME

In connection with this work it seemed desirable to ascertain the action on the penis of certain drugs which influence the systemic blood pressure and especially the peripheral vessels.

There are very few available data as to the effect of drugs on the vascularity of the penis. Hunt has shown that acetyl cholin dilates the dog penis, especially after ligation of the coeliac axis, mesenteric and renal arteries, that this was abolished by atropin, and that nitroglycerin caused dilatation of the penis and hind limb, that small amounts of epinephrin caused its contraction, while large amounts caused passive dilatation (89).

Nikolsky claims that small amounts of camphor lessen the flow from the dorsal vein of the penis, while large amounts increase it (90).

Atropin, not only paralyzes the ends of the cardiac vagus fibers, but seems to act on some portion of the heart beyond the vagus, hence the intravenous injection into dogs sometimes causes a fall in blood pressure. In one dog, where such injection caused this fall it lessened the penis volume, but in another dog in which it raised the blood pressure it caused marked dilatation of the penis. According to Nikolsky, the injection of 0.01 gram of atropin sulphate paralyzes the ends of the Nervi erigentes, the vaso-dilator nerves for the penis (91). Even after the injection of 0.5 mgm. atropin sulphate, an extract of testicular substance (3 grams) caused a fall in the systemic blood pressure. Using large amounts of atropin and small amounts of testicular substance, Dixon found that atropin prevented the fall in blood pressure.

One tablet of Yohimbin (0.005 gram) produced a marked fall in blood pressure (dog 15 kilos), marked vaso-dilatation of the fore limb and very slight dilatation of the penis. This stands in line with the clinical reports as to its inefficiency as an aphrodisiac.

The intravenous injection of the fluid extract of Muirapuama (1 cc.) into a dog 24 kilos produced no change in the volume of the penis. In another dog the fluid extract of Muirapuama (5 cc.) caused marked cardiac inhibition with a transitory fall in

blood pressure, a transitory constriction of the fore leg and no noticeable effect on the penis volume.

Infundin (one ampoule) caused a slight initial dilatation, followed by a fall in volume of the hind leg; a rise in blood pressure with an initial rise in penis volume, followed by constriction (curve IX).

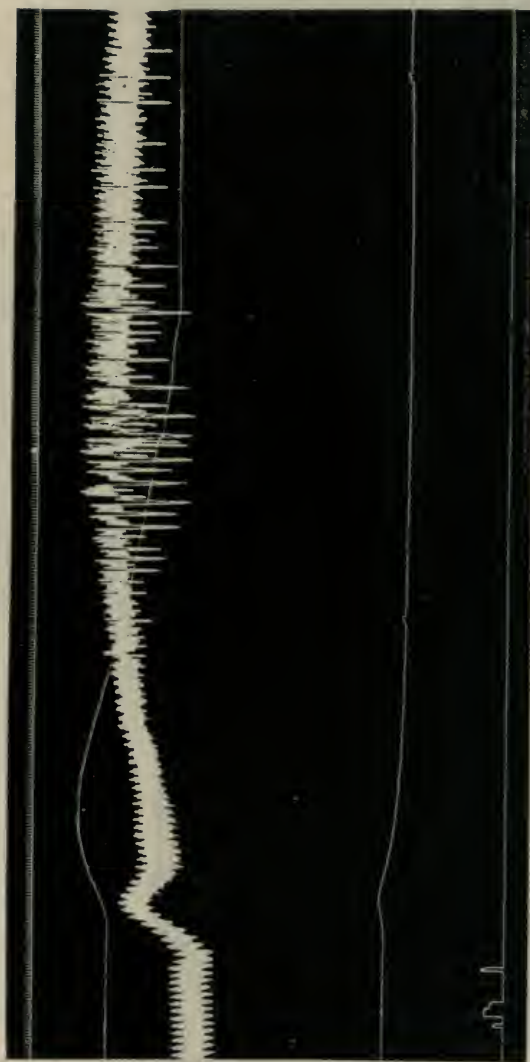
Histamin is believed by Abel and Kubota to be the compound which is mainly responsible for at least, part of the fall in blood pressure produced by extracts of various organs (92) and Hooker has shown that besides dilating the capillaries of the body (93); it also dilates the venules (94). Histamin (0.04 mgm). produced an initial slight constriction of the penis and subsequent dilatation. The fore leg dilated slightly (dog 24 kilos). In another dog (18.5 kilos) the penis constricted, then as the hind leg dilated, it dilated (curve X). Large amounts, 1 mgm., cause constriction of fore leg and marked dilatation of penis.

Nitroglycerin (1.3 mgm.) caused a marked fall in blood pressure, first a constriction, then a dilatation of the fore leg and slight dilatation of the penis. The injection of the emulsion of one dog testis then caused a marked dilatation of the penis. In a dog (24 kilos) the intravenous injection of 1 cc. of the tincture of cantharides produced a marked constriction of the penis with some slight constriction of the hind leg, but with little, or no effect on blood pressure (curve XI).

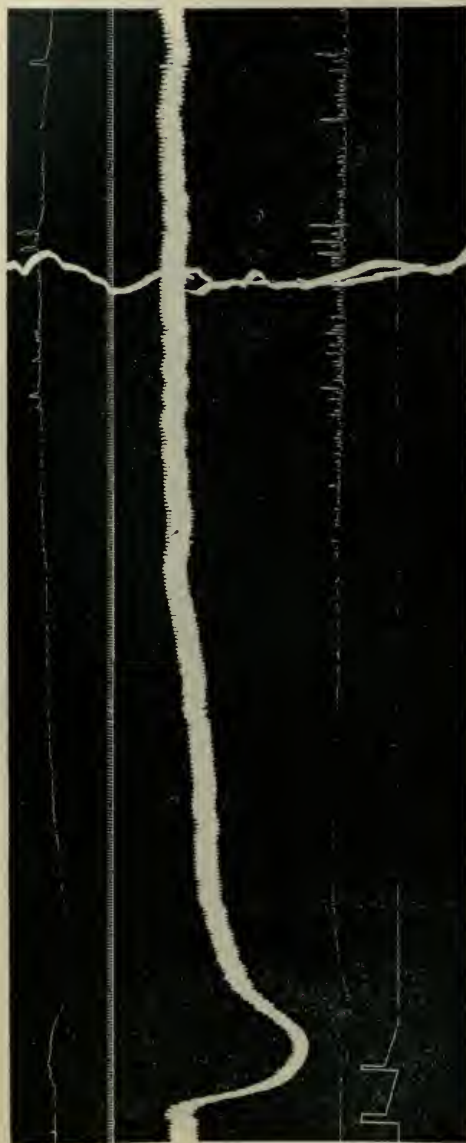
Strychnin sulphate (2 mgm.) on intravenous injection into a dog (24 kilos) caused a delayed dilatation of the penis after twelve minutes, with slight, if any dilatation, of the hind leg. The blood pressure rose very slightly, then fell, even while the penis was dilated (curve XII). A second experiment on another dog failed to give this marked rise in penis volume.

CONCLUSIONS

1. There seems to be in the testes a specific dilator for the penis.
2. Agents which dilate the blood vessels of the hind limb increase to some extent the volume of the penis.



CURVE IX. DOG (24 KILOS). ONE AMPOULE (1 CC.) INFUNDIN
Penis, upper line; hind leg, lower line

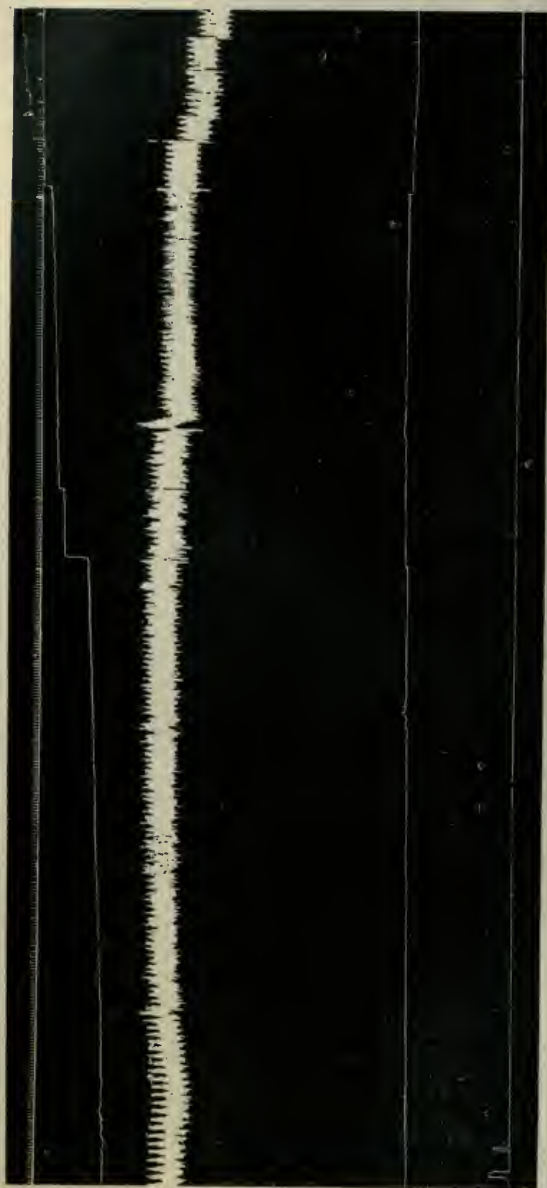


CURVE X. HISTAMIN 0.04 MGM.

Lower curve left hind leg. Upper line penis. Dog (18.5 kilos)



CURVE XI. Dog (24 KILOS). TINCTURE CANTHARIDES (1 CC.) INTRAVENOUSLY
Top line, penis; lower line, hind leg



CURVE XII. DOG (24 KILOS). STRYCHNIN SULPHATE $\frac{3}{8}$ GRAIN (2 MGM.) INTRAVENOUSLY

Machine stopped to save paper—rise at points of stoppage more evident. Penis, upper line; hind leg, lower line.

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GIANT VESICAL CALCULUS

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Giant calculi in the present day of surgery are so rarely seen that one expects such only from some distant civilization or under extraordinary circumstances. That the case about to be reported should have developed in the midst of the medical activities of Philadelphia is in its self unique. That it represents the largest vesical calculus authentically reported to have been found ante-mortem and in all probability the largest in medical literature demands that a full report be made of the case.¹

J. F. M. Age sixty-one. White. Male. Foreman carder in a woolen mill.

Family history. Negative for tuberculosis, malignancy, or other hereditary complaint.

Past history. Married and the father of ten children, the youngest being but four years old. No acute infectious diseases since childhood. No operations. Twelve years ago the patient passed by urethra three very small calculi. This was followed by frequency of urination, a symptom that has persisted to the present time with but slight variation. He has noticed that urine on standing would form a crystalline deposit on the vessel wall. Hematuria was noticed several years ago but none recently. Patient has had for many years a right inguinal hernia, for which he has worn a truss and his last examination by a physician was in regard to this condition in December, 1918, at which time he was having increasing difficulty in restraining his hernia. He complained to his family that "his bowels were knotted up and as hard as stone." At the same visit he sought advice for constipation

¹ This specimen was presented before the Philadelphia Genito-Urinary Society, March 22, 1920, by Dr. E. E. Keiser, from whose patient it was removed. Dr. Keiser allowed the author to present it before the American Urological Association that same week and has since kindly consented to deposit it in my care in the Museum of Pathology, Department of Urology, University of Pennsylvania.

and hemorrhoids; apparently no examination of his abdomen was made at that time and he continued at his work until July 3, 1919.

Present illness. At the above date in July, 1919, the patient discontinued his work because of his suffering from hemorrhoids and his inability to properly support his inguinal hernia. He was likewise losing strength. His condition, however, was not so severe as to prevent him from visiting New York on July 12, 1919, accompanied by his spiritual adviser, in the hope of procuring a special make of truss to better support his hernia. To the credit of the truss specialist, he was told that he needed a surgeon, not a truss, and Dr. E. E. Keiser was called to see him on July 17, 1919.

Physical examination. On examining the abdomen a hard tumor was found extending from the symphysis pubes almost to the umbilicus. It was fixed solidly in place and perfectly immovable, apparently a part of, or firmly attached to, the pelvis. On passing a silver catheter no obstruction was found in the urethra and it entered without difficulty a short distance into the bladder. About $1\frac{1}{2}$ ounces of clear urine were withdrawn, examination of which showed no albumin, no sugar, and no macroscopic evidence of blood. On entering the bladder the catheter grated upon a hard surface which was believed to be a calculus. Roentgenologic examination by Dr. W. H. Morrison showed an immense shadow filling entire true pelvis and extending three finger breadths above the line of the sacral promontory. Because of the size and immobility of this mass it was thought that it might be an osteoma arising from one of the pelvic bones. The patient was in a very weakened condition and operation was deferred in the hope of building him up. Obtaining but little response or improvement in three weeks it was deemed advisable to proceed.

Operation. August 11, 1919. Suprapubic cystotomy.

The bladder was opened without injury to the peritoneum. It is needless to point out the difficulties the operation entailed. The calculus was firmly fixed in the pelvis. The walls of the bladder were markedly thickened and its inner surface bore but little resemblance to the normal mucous membrane. The calculus was removed without visible injury to any important structure and the bladder closed about the usual tube and gauze drainage. The patient died thirty-six hours after operation.

Specimen. The stone weighed on delivery in its moist state exactly 64 ounces, or 4 pounds; at present it weighs 56 ounces, or $3\frac{1}{2}$ pounds. Its longitudinal circumference measures 48 cm. and its greatest hori-



FIG. 1
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zontal circumference (that above the brim of the pelvis), 40 cm. The mark of the superior straight is very evident, while the portion opposed to the symphysis has formed an overlapping ledge (X) and is quite ebonized. Posteriorly can be seen the imprint of the outline of the sacrum, grooved on the left by a shallow depression showing the course of the rectum. Below on the right is a teat-like projection (Y) under which in pulley fashion can be seen the curve of the course of the right ureter. The surface is generally quite smooth, of dark brown color, and in spots appearing polished. Where this surface has cracked off there is exposed the soft, white, granular material characteristic of calcium phosphate deposit. On the portion under the projecting ledge that was approximated to the symphysis the surface is of especially high polish resembling ebonized bone. The calculus has not yet been sectioned.

With such an unusual specimen one immediately desires to know whether it represents the record for human vesical calculus formation.

I have carefully searched the literature and have been unable to find any report of a stone of equal or greater size having been removed by operation. Of recent literature may be mentioned the report of Mitchell in 1915, before the New England Branch of the American Urological Association, of a successful lithotomy for a calculus weighing 30 ounces. Emerson C. Smith (1) reports the successful removal of a stone weighing $38\frac{1}{2}$ ounces, and states after a careful survey of the literature, that up to the time of its removal this was the largest stone removed with the recovery of the patient. I likewise have been unable to find any report of a successful lithotomy of a greater size than these.

A review of Ashurst's International Encyclopedia of Surgery; Sir Henry Thompson's Catalogue of Collection of Calculi; The Catalogue of the Royal College of Surgeons; Freyer; Coulson; Ebstein; the current text books of Urology, and other books dating back through the nineteenth century, give numerous remarkable specimens, either found post-mortem or in which death followed operation, varying in weight up to 51 ounces, but none to exceed this specimen. I have found two references to vesical calculi of greater size than my specimen.

1. Anomalies and Curiosities (2) state that de Buffon records a vesical calculus weighing 6 pounds. I have instituted a thorough search for this reference with the following results. George Louis Le Clerc, Comte de Buffon (1707-1788), was a voluminous writer on natural history. The reference is to a 6-volume, Brussel's edition of 1828-1833, no page or volume reference is given. I obtained this from the Surgeon General's Library to find it composed of 14 volumes of text and 6 of illustrative plates. A most painstaking search failed to reveal the reference. I obtained this edition in order to leave no stone (!) unturned, for before doing so I had already searched three sets of de Buffon's complete works, (a) a 14-volume edition, Paris, 1774-1779, (b) 13-volume edition, Paris, 1775-1789, and (c) a 16-volume edition, Paris, 1853, all of which are in the Library of the College of Physicians, Philadelphia; as likewise a 127-volume edition, Paris, 1819, and other miscellaneous books of his in the Library of the Academy of Natural Science, Philadelphia. As I have stated de Buffon was essentially a natural scientist; in the 127-volume edition but four volumes are given to man, and in the 14-volume Brussel's edition, but one is devoted to the genus *homo*. However, the entire works were searched with the consideration in view that possibly the calculus was other than human, and though bezoars from the horse, buffalo, goat, rhinoceros, and elephant are described weighing, in the latter, 8 pounds 15 ounces and 6 grains, the largest human vesical calculus mentioned is 7 ounces 6 drams and 28 grains (vol. v, p. 318). Considering that the original reference was incomplete as to page and volume, incorrect as to number of volumes in the edition, that four of the five editions searched were published after the death of de Buffon, making it impossible that a later observation was not included, and that my search revealed no reference to such a calculus, I am forced to the conclusion that de Buffon has been misquoted and that such a calculus did not exist.

2. Sir Jonathan Hutchinson (3) cites Morand as having seen a calculus weighing 6 pounds; he however states that it was removed postmortem. Hutchinson gives no reference. Again a search of Morand's writings has developed the following results.

The reference is undoubtedly to the famous French lithotomist, Sauveur-François Morand, born 1697 and whose death occurred in 1773, a contemporary of de Buffon. Morand's Dissertation on the High Operation for the Stone (1729) does not mention such a calculus. His little treatise entitled *Recueil pour servir d'eclaircissement la Malaide d' Fille de S. Geomes* (1754) contains no mention of the above observations, though citing several remarkable histories. His *Opuscles de chirurgie* (1768-1772), though catalogued in the Suregon General's Index, Colonel Garrison tells me has been lost from the Library. However, I was fortunate to get the German translation of this through the courtesy of the New York Academy of Medicine, edited by Ernst Platner, Leipzig, 1776. Over a third of this work of 450 pages is devoted to a most thorough exposition of calculus disease, it being finished just prior to its author's (Morand's) death. It contains no mention of such a giant calculus, nor anything to exceed in size my specimen.

Coulson (4) makes the following comment.

The largest calculus on record is said to have been in the possession of the French lithotomist Morand. It weighed 6 pounds 3 ounces. This may be apocryphal, but the one recorded by Deschamps is authentic. This enormous stone, which weighed 51 ounces, was extracted after death from the bladder of a poor curate, who died in the hospital of La Charite, Paris, in the year 1690. It was $6\frac{1}{2}$ inches long and 1 foot in circumference. Deschamps weighed it after the lapse of a century and found that it had lost in weight only 2 ounces and $\frac{1}{2}$ drachm. The largest calculus in our (British) collections is the one which the late Mr. Cline attempted to extract from the bladder of Sir Wm. Ogilvie. This calculus was larger than the one mentioned by Deschamps, though not so heavy; it weighed 44 ounces and was 16 inches around one axis, and 14 inches around the other.

So as regard to Morand's giant calculus I am forced, after a complete, though unproductive, search, to concur with Coulson that "this maybe apocryphal." Certain it is that if it did exist it was removed post mortem (as recorded by Hutchinson).

It is of interest to note here that these two references to so similar a specimen find a common meeting ground between the two authors in the following reference from de Buffon (5) descriptive of article 1358, Cabinet du Roi, as follows:

Part of a concretion extracted from the caecum of a Man. . . . This piece had been sent to the hospital from Nantes by M. Morand, the father, in 1752: It is accompanied by a note which shows that it formed part of a concretion of considerable volume, which was fastened to a bone, and that the other portions of the same concretion contained some cherry stones. This portion is a sort of hair-ball (egagropile) of hard felt, composed of very fine yellow filaments; it envelops almost entirely a piece of bone, of blackened color on the outside; it all is very light and of about the size of a flattened face.

My conclusions following this painstaking search of the literature, are that this represents the largest specimen of human vesical calculus formation of authentic record, certainly the largest removed during the life of its host and a specimen so unique that it will probably stand in a class by itself for all time.

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CLINICAL INVESTIGATION OF THE PHENOLSULPHONEPHTHALEIN TEST

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In a consideration of the phenolsulphonephthalein test it is apparent that with the actual impairment of kidney function, either by destruction of kidney tissue or by the impaired functioning of the normal amount of kidney substance, the amount of phenolsulphonephthalein excreted would be diminished. The question arises, however, whether in all cases of low phenolsulphonephthalein output the kidney is the only factor involved. If the dye is injected intravenously, the substance reaches the kidney in a very short time and its excretion begins within two minutes or less; if it is injected subcutaneously the delay of its appearance is longer. If conditions should exist within the body whereby the injected phenolsulphonephthalein is absorbed and retained in its transit to the kidney, this action might result in delaying or indefinitely holding up a certain amount of the dye, so that the problem is not one of whether the kidney can or cannot excrete it, but whether or not the kidney has a chance to excrete it.

If two persons are in the same condition as regards the factors, other than the kidney, influencing the phenolsulphonephthalein excretion, the test, as ordinarily applied clinically, is a measure of the kidney efficiency. If, however, two persons differ in the factors other than the kidney, the diminished phenolsulphonephthalein output would be explained solely as impaired function of the kidney, and the test as applied today would not take into consideration the influence of these factors. Our attention was called to the factors other than the kidney while carrying out experimental work concerning the metabolism of sugar and amino acids in dogs. It was found that the type of food and the

capacity of each animal to carry out the reactions occurring in the metabolism of sugar and amino-acids, are factors determining the phenolsulphonephthalein output. Although the body, as a whole, eliminates phenolsulphonephthalein in a surprisingly high degree, the relatively large amounts of tissue other than kidney have some upper and lower limits of saturation which must be satisfied before the kidney even begins to excrete the dye.

Beside the mere retention of phenolsulphonephthalein by the tissues, another question which must be determined is whether any of the dye can be actually destroyed within the body and thereby be removed from possibility of excretion by the kidney. It may readily be shown that phenolsulphonephthalein can be destroyed by being mixed with the body tissues *in vitro* in the absence of oxygen. The presence of oxygen prevents its destruction. If, in the animal organism, similar conditions of lack of oxygen could arise, the phenolsulphonephthalein would be destroyed in the tissues *in vivo*. A clinical investigation was, therefore, undertaken to determine to what extent factors other than the kidney can be proved to affect the phenolsulphonephthalein output.

In considering the destruction of the phenolsulphonephthalein within the tissues, while it may be shown that this occurs *in vitro*, our results indicate that a very profound degree of cyanosis must exist before this condition occurs clinically. Low hemoglobin in itself apparently does not reach such a low point that it alone is sufficient to cause a destruction of phenolsulphonephthalein within the tissues. Decompensation and cardiac insufficiency must proceed to such an extent that the patient is clinically in a crisis before this factor comes into play. Impairment of lung capacity to a point of deep cyanosis is necessary before the tissues can be sufficiently impoverished, with regard to oxygen, so that phenolsulphonephthalein is destroyed. These results may be briefly stated that clinically the destruction of phenolsulphonephthalein within the tissues in explaining low phenolsulphonephthalein output can be excluded in any cases in which a condition of cyanosis is not obvious to the eye. That

destruction is probably involved in terminal cases with marked cyanosis, seems highly probable, but if the patient is able to be up and about it is doubtful whether destruction of the dye within the tissues plays a very important part in the lowered phenolsulphonephthalein output.

In experimenting with animals, it is impossible to recover the dye from the tissues if a very long interval has passed after the injection of the substance and the death of the animal before it is attempted to determine the amount of phenolsulphonephthalein left. The destruction of phenolsulphonephthalein within the tissues not properly oxygenated is rapid and complete.

In investigating the possibility of the retention of phenolsulphonephthalein in tissues other than the kidney, so that the low phenolsulphonephthalein excretion could be explained by factors other than the kidney, some interesting results have been obtained. With regard to the mode of injection, it has already been pointed out that phenolsulphonephthalein is absorbed from the tissues more slowly after subcutaneous injection than after intravenous injection, and it has been shown that after injections into different parts of the body, the time of absorption varies. The influences controlling the absorption from the site of injection, however, are not entirely clear. In a normal person the phenolsulphonephthalein output, determined after subcutaneous injection, allowing two hours for the excretion of the dye, may be identical with the phenolsulphonephthalein output following intravenous injection. In another case, the total amount excreted after a subcutaneous injection may be the same as after intravenous injection, but the time required is very much longer than two hours.

It was observed that in patients with urinary obstruction of longstanding, who were being prepared for operation, the two-hour phenolsulphonephthalein return following intramuscular or subcutaneous injection was frequently lower than other clinical data would indicate. When the phenolsulphonephthalein was injected intravenously, the two-hour output was found to be much higher. This difference was particularly marked in patients undergoing preliminary treatment for prostatectomy

who were suffering from or had recently recovered from the reaction following drainage. Even though the patient's general condition improved, it not infrequently happened that the two-hour phenolsulphonephthalein return remained at an abnormally low level following intramuscular injection. If, however, intravenous injection was made, the output was frequently much higher and often almost normal. In practically every case the return from the intravenous injection was considerably higher than the intramuscular. It is evident that there must be some condition in the tissues of the patients in this group which prevents the normal absorption of phenolsulphonephthalein in the first two hours following intramuscular injection. It would be logical to assume that the phenolsulphonephthalein return following intravenous injection will give a more accurate index of renal function in the presence of urinary obstruction than following intramuscular injection. The phenolsulphonephthalein return after intramuscular injection will afford a rough index of the degree of chemical changes in the tissues as a result of urinary retention or infection, and will frequently give a fairly accurate appraisal of the patient's general condition.

Following the previously reported observation of one of us (Kendall) that if the tissues in dogs are rendered alkaline, phenolsulphonephthalein will be more readily given up, we endeavored to corroborate this in man. By giving the patient enough sodium bicarbonate by mouth to render the urine alkaline, a partial degree of alkalization is probably attained. It was found that after alkalization of the urine the phenolsulphonephthalein output was increased from 10 to 50 per cent, largely in patients suffering from urinary obstruction or renal infections, in other words, when the impairment in renal function was temporary and dependent on these factors. Whether this is explained in full by the slight alkalization of the tissues with attending changes in the power of the tissues to retain the dye, is unknown, but this seems a very probable mechanism.

If, however, there is permanent impairment of the renal cells such as occurs with advanced chronic nephritis, but little difference is found in the phenolsulphonephthalein output following

intramuscular and intravenous injection, both being low. With nephritis the renal cells are actually diseased to such an extent that their functional capacity and power to excrete the dye are limited. In such cases it is a mechanical impossibility for the renal cells to excrete more rapidly, and as a result the dye is either destroyed in the tissues before it can all be excreted or is eliminated through other channels. Even though the tissues are alkalinized there is little or no increase in the phenolsulphonephthalein secretion, which is in marked distinction to the results observed in the clinical condition following urinary obstruction. In the latter condition the renal cells, being unimpaired, are able to excrete the increased amount of dye liberated by the alkalinized tissues.

The condition of the circulation of the blood may also influence the excretion of the dye. Rountree and Geraghty noted that in cardiac insufficiency the two-hour phenolsulphonephthalein output was frequently greatly reduced and so caused confusion with renal disease. They stated that with rest in bed, cardiac stimulants, and so forth, in the course of time the phenolsulphonephthalein output increased to normal if the cardiac condition was the etiologic factor, but remained subnormal if renal disease existed. In one series of patients with circulatory insufficiency the primary absorption of phenolsulphonephthalein was retarded when given intramuscularly. If given intravenously, however, this factor is overcome and the two-hour return is normal if no advanced renal disease is present; thus a ready method of differentiation is offered. Furthermore, in the presence of combined cardiac and renal insufficiency the relative degree of cardiac insufficiency may be inferred by the difference between the two-hour return following intravenous and intramuscular injection.

CONCLUSIONS

1. It is difficult to corroborate, clinically, the fact that phenolsulphonephthalein is destroyed in the tissues unless it is protracted by sufficient oxygen, since such a profound degree of cyanosis would necessitate impending death.

2. The clinical problem involved in the phenolsulphone-phthalein test may not be alone whether the kidney itself is capable of excreting it but whether the kidney has the chance to excrete it.

3. Patients with urinary obstruction undergoing preparation for prostatectomy will frequently have a low phenolsulphone-phthalein output following intramuscular injection and a normal output following intravenous.

4. The intramuscular injection probably gives a more accurate index of the condition of the tissues, but the renal capacity is best estimated after intravenous injection.

5. When true nephritis with actual destruction of renal cells exists there is but little difference in output following intramuscular and intravenous injection.

6. The extent to which phenolsulphonephthalein is retained in the tissues is influenced by the degree of acidosis. If rendered alkaline the tissues will readily liberate it.

7. Following alkalization of the urine the phenolsulphone-phthalein output with intramuscular injection is apparently higher.

8. With nephritis alkalization of the urine has but little effect on the output.

9. In the presence of cardiac insufficiency accurate estimation of the renal function is obtained best by intravenous injection. The difference between the intramuscular and intravenous output offers a fair index of the comparative degree of cardiac and renal impairment.

TRANSACTIONS OF THE NEW ENGLAND BRANCH OF THE UROLOGICAL ASSOCIATION

The thirteenth annual meeting of the New England Branch of American Urological Association was held at the Harvard Club of Boston on November 16, 1920, with Dr. O'Neil presiding.

The following officers were elected:

President: Dr. J. W. Keefe.

Secretary and Treasurer: Dr. G. G. Smith.

Executive Committee: Maine, Dr. Alfred Mitchell, Portland; Vermont, Dr. W. W. Townsend, Burlington; Massachusetts, Dr. J. D. Barney, Boston, Dr. I. N. Kilburn, Springfield; Rhode Island, Dr. C. O. Cooke, Providence.

There were elected to membership: Dr. H. A. Chamberlain, Boston; Dr. H. H. Crabtree, Boston; Dr. H. Groeshinsky, New Bedford; Dr. P. N. Pappas, Boston; Dr. C. N. Peters, Portland, Maine; Dr. A. Riley, Boston; Dr. D. E. Shea, Hartford, Conn; Dr. W. L. Wright, Boston.

PRESENTATION OF SPECIMENS AND REPORTS OF CASES

Dr. A. L. CHUTE: I wish to show an interesting kidney that I removed this morning. The patient was a married woman, thirty-two years old, who had had one child; her symptoms, those of a mass in the right side of her abdomen and digestive distress, going back for eight years, but for two years past they have been more pronounced. She presented herself for investigation about a week ago. On palpation I could feel in the right side of her abdomen, well below the costal border, a mass, hard, round, and smooth, about the size of a baseball. It seemed to extend back into the loin but was so movable that it could be displaced beyond the median line.

There had never been any hematuria and her urine at the time of my examination was absolutely negative (transparent, 1.018, no blood, no leucocytes). The probable diagnosis of a distended gall-bladder had been made some years before. The urine was said to have shown bile on one occasion.

It seemed probable to me that the mass was a kidney—the ability to displace it back into the loin I felt was most suggestive. Pyelograms showed the marked pelvic deformity seen in the plate. The distortion was suggestive of hypernephroma but not typical. There has been no pathological examination of the specimen as yet but I fancy it will prove to be a hypernephroma that is not proliferating actively; possibly it may be a sarcoma.¹ The interesting features of this case are

¹ Pathological examination showed this to be a hypernephroma.



FIG. 1. PYELOGRAM OF DR. CHUTE'S CASE



FIG. 2. PHOTOGRAPH OF KIDNEY DESCRIBED BY DR. CHUTE



FIG. 3. INJECTED X-RAY OF KIDNEY FROM DR. CHUTE'S CASE, AFTER REMOVAL

the great mobility of the mass (it could be displaced beyond the median line); the lack of symptoms, such as hematuria or pain, one or the other of which we rather expect to see in tumors of the kidney, and the long time (eight years) that this tumor has been quiescent.

Dr. R. F. O'NEIL: Did you remove it through the loin?

Dr. A. L. CHUTE: No. I went through the peritoneum incising the posterior layer of the peritoneum outside of the ascending colon and displacing the latter inward so as to get a good exposure. The kidney mass was so tipped that the pelvis was where the upper pole should have been; the pedicle seemed to come off from here. There were all sorts of adhesions and you could see one large vessel that came off below.

Dr. J. W. KEEFE: In regard to those movable kidneys I recall one that you could move to the left of the median line. The books tell us if a mass is a gall-bladder you will have continuous dullness from the liver downward and I feel that is usually one of the distinguishing features, though in the case in point one might well make a mistake as to whether it was kidney or gall-bladder. This kidney I removed by the transperitoneal method.

Dr. CUNNINGHAM: I have here an X-ray plate which to me is unusual. It is unusual inasmuch as the ureters may be traced throughout their course from the kidney to the bladder on both sides. Nothing has been injected into these ureters. I think the case is one of double pyelonephritis in a man, forty-five years old, who has run a temperature up and down, up to 104° and down to 99° for the past three months, never getting down to normal. He was supposed to have had some focal infection. He was sent to Dr. Joslin in consultation, who could find nothing except a questionable palpable spleen. There were no abnormal urinary signs except that the urine showed a few pus cells, a few blood corpuscles and abundant urates. About a week before I saw him he began to have a slight pain in the left kidney region which radiated to the left testicle and the pain in the testicle has persisted and has become so severe that it requires morphia to control it.

Those who have been caring for this patient have exhausted all methods of diagnosis, both by physical examination and laboratory tests, all of which, including three blood cultures, are negative. He has had three teeth removed because of questionable pus at the roots, but without benefit. The patient's general condition is gradually failing, having dropped 20 pounds in weight during the past three months.

He was sent to me to find out the explanation for the pain in his testicle. The general physical examination was negative, the external genitals, and the prostate and vesicles normal by all tests. The cystoscopic examination showed he had a normal bladder capacity, a little

edematous change in the mucous membrane around the left ureter. Both ureters were catheterized, the urine from each side showing a very small amount of pus, with a few red blood corpuscles, and the phthalein output was 14 per cent from each side, in fifteen minutes from an intravenous injection, and 2 per cent was recovered from the bladder, so that the kidneys do not seem much involved. The X-ray plates of the kidneys are negative, but if you can see in this light, you will notice the ureters on both sides very distinctly; they are enlarged in circumference, and there seems to be a dense line of deposit in the outer wall, while the lumen shows nothing. To me it is a unique thing, and I wonder if any present have seen such a thing before and what you may make of it.

Dr. R. F. O'NEIL: Nothing that suggests tuberculosis?

Dr. CUNNINGHAM: We are running it through the guinea-pig test with that in mind. The smears are negative.

Dr. G. G. SMITH: You make those ureters out to be very much dilated?

Dr. CUNNINGHAM: I do.

Dr. G. G. SMITH: I saw a case in the Massachusetts General Hospital of a man who had a tremendously dilated ureter of about that size. I supposed it was due to a strictural condition at the lower end, though one could get a catheter into it. His ureters did not show in the X-ray without an injection, but they were dilated in the same way as these.

Dr. HORACE BINNEY: This is an illustration of a case seen in the hospital in which I was serving during the war, representing an injury to a branch of the renal artery. I thought it might be of interest to this Society. The patient, a British soldier, was shot in the right flank rather far back, and the case came down to our hospital which was some forty miles back of the casualty clearing stations, where such cases were usually operated on if regarded as severe. Apparently the man when first seen had no definite sign of injury to the kidney, and there was no record of an X-ray. When he came down to us a day or two later he was in considerable shock and had a small amount of blood in the urine. There was no other evidence of renal injury. The X-ray showed a machine gun bullet resting on the vertebral column—I do not recall the exact location—but so high you would not have expected it to injure the renal artery. The man became worse rapidly and died, and autopsy showed a machine gun bullet, as I recall it, between the vertebral column and the vena cava at a higher level than the renal artery and the hilum of the kidney. The wound of entrance being relatively high we had figured before that the bullet must not have seriously injured the kidney. The autopsy showed it had done so, and that apparently the

conditions of the man's anatomy at the time were such that the kidney was pushed up, and the bullet pierced a branch of the renal artery, causing an infarct of quite a large part of the kidney. I do not think that we were able to decide what caused death. I should not think that the injury to the kidney would be so rapidly fatal. It is possible that the pressure by the bullet on the sympathetic nerves near the solar plexus may have been the cause of death, perhaps from prolonged shock.

Dr. A. H. CROSBIE: I have some radiographs of a case of diverticulum of the bladder which might be interesting to pass around. There is nothing especially new about it. It was a large diverticulum which lay posteriorly behind the bladder tightly glued to the rectum and was almost as large as the bladder itself. One of the interesting things about it was that it was a man, fifty-nine years old, and at the time the diverticulum was removed, the bladder outlet felt tight and it was evident that there was some obstruction there, but he had lost some blood during the operation, and I waited until the wound healed up, and after the bladder wound healed the patient had a residual of 8 ounces. Previous to operation he had complete retention. I then went in and did a perineal prostatectomy and removed a fibrous prostate, and he now empties his bladder completely. One of the radiograms showed a lateral view, and from the lateral view you can get an idea of the size of the diverticulum compared with the size of the bladder.

Dr. W. C. QUINBY: I recall in this connection a case entirely similar to the one Dr. Crosbie has related, of extensive diverticulum arising from the floor of the bladder just above the interureteric bar, and extending downward between the bladder and rectum to which it was densely adherent. This occurred in a bladder which was also obstructed by an hypertrophied prostate. I removed the prostate first by enucleation, and was pleased to find that the loosening of the normal attachments of the bladder neck, caused by this procedure, was of the greatest aid in facilitating enucleation of the diverticulous sac.

Dr. BIERBACH: I had a case of profuse hemorrhage from the bladder and I cystoscoped him at my office and found that the bleeding was coming from the right kidney. The patient was sent to the hospital and there again cystoscoped. The bladder showed a marked trabeculation, with a pearly-grey appearance of the mucous membrane, and the right ureter was sending forth a steady stream of blood. Each ureter was catheterized, and the catheter passed freely to the pelvis on both sides. Bloody urine appeared from the right, and clear from the left. The catheter on the right side moved freely when within the pelvis, and the pyelogram showed by its position that the pelvis was well dilated. The Wassermann blood serum test was strongly positive. A diagnosis of gumma of the right kidney was made by elimination. The patient was given 0.3 gram of arsphenamine of the state board

product, and the bleeding on the following day subsided. Following this three more injections were given, one every four days, and the urine became macroscopically free from blood. The patient has now been back to work for some time, feels well, and is free from any further symptoms of bleeding. The pyelogram shows a marked dilated kidney pelvis, probably due to gumma formation.

Two Cases of Pneumaturia Due to Diverticulitis of the Sigmoid. ROGER C. GRAVES. From the Urological Clinic of the Peter Bent Brigham Hospital. (By invitation.)

Cases of chronic colon bacillus infection of the urinary tract with excessive pyuria, are of too frequent occurrence to be of striking interest. We meet them daily in all their varied forms and degrees of involvement. When, however, pneumaturia is reported as an associated symptom, and gas is passed with the urine, the situation assumes a new significance. The necessary differential diagnosis is interesting and is extremely important.

Excluding those temporary babbings which may follow the introduction of a hollow instrument into the bladder, the passage of gas through the urethra may result from the activity of gas producing organisms: the colon bacillus, the bacillus aerogenes capsulatus, or a yeast fungus. Such pneumaturia usually occurs in a sugar containing urine, the gas being the direct result of fermentative change. We have very recently seen a diabetic patient whose urinary tract was chronically infected and who complained of bubbling urination. Cases of that type are not at all infrequent. Patients will be seen, however, for whom so simple an explanation will not suffice, and it must then be borne in mind that the gas which they pass per urethram has its origin, in all probability, outside the urinary system. In such cases, pneumaturia must be accepted as evidence of the presence of a fistulous communication between the intestinal and urinary tracts. An accurate diagnosis is of the utmost importance, and surgery affords the only hope of relief.

The two following cases will be of interest:

Case 1. Peter Bent Brigham Hospital. Surgical no. 12785.

An American civil engineer, married, age sixty-seven, entered the hospital on July 13, 1920, complaining of cloudy urine. The family and marital histories were not important. The patient was born in Vermont. He had lived in New England for the past twenty-five years. He had never been physically strong, but there had been no recent serious illness. He had the usual childhood infections with diphtheria and scarlet fever in early life. He had erysipelas and "typhoid-pneumonia" many years ago, and malaria at the age of twenty-eight. He had occasional periods of palpitation and slight dyspnea on exertion. He had always been constipated but recently his bowels had moved daily without catharsis. Average weight 120 pounds; present 115 pounds.

Several months before admission the patient consulted a physician because of loss of weight. He had no other complaints. No diagnosis

was given him. Three weeks before coming to the hospital he noticed that his urine was brown in color and cloudy. It contained brown flakes of material suggestive to him of clotted blood. These changes were persistent. There was at first slight burning in the urethra at the end of urination but this subsided. There had been very slight increased frequency and some urgency. Bubbles of gas had been passed with the urine. Backache across the lower lumbar region was experienced on one day only. There had been no difficulty in starting the stream and no diminution in its size; no sense of residual urine, no incontinence, no unmistakable blood in the urine, no actual pain, no chills or fever. The appetite had been fair, the patient had slept well. He complained, however, of a loss of energy during the past several months and of a loss of weight during the past year, of 18 pounds.

Examination found a well developed and undernourished adult male of advanced years who lay comfortably in bed without evident distress or pain. Temperature, pulse and respirations: normal. The general physical findings were not remarkable. The liver edge and lower pole of the right kidney were palpable, the abdomen was otherwise negative. There was no costo-vertebral tenderness. Urine: yellow, cloudy, acid, 1.008, slight trace of albumen, no sugar, many pus cells. Phthalein excretion in two hours: 35 per cent. Hemoglobin: 80 per cent. White blood count: 22,000. Blood Wassermann: negative. Cystoscopic examination found evidence of rather marked cystitis. In the mid-line posteriorly, above the trigone, was a small discrete, reddened area, raised and uneven in appearance, and apparently inflammatory in nature. Pus was found in the bladder and right kidney urines. There was no flow from the left side. A colon bacillus was grown in culture. X-ray studies and pyelograms were negative.

Believing the condition to be one of chronic infection, pelvic lavage was begun. The patient had a very sharp reaction to treatment. There followed a prolonged period of fever, and several days of stubborn diarrhea which was believed to be a concomitant of the fever and toxemia. The urine continued to be exceedingly cloudy. Further cystoscopic treatments were of course impossible at the time, but bladder lavage was given daily in an attempt to combat the marked cystitis. The patient made little progress; he did not gain strength; the fever continued and the urine became so foul that it was fecal in both appearance and odor. In an attempt to find a bladder fistula a cystoscopic examination was performed but in the presence of rampant infection a satisfactory study could not be made. A barium enema was ordered with the interesting result that several hours later barium was passed through the urethra. The X-ray plate showed a definite irregularity in outline in the lower portion of the sigmoid. With a diagnosis of vesico-sigmoid fistula due to carcinoma or diverticulitis, operation was performed. A chronic inflammatory condition, diverticulitis, was found to be present in the lower sigmoid. Attachment to the bladder had taken place with subsequent communication between the two structures.

Case II. Peter Bent Brigham Hospital. Surgical no. 12948.

A Canadian merchant-tailor, married, aged sixty-four, entered the hospital on August 11, 1920, complaining of backache, cloudy urine, and the passage of gas through the urethra. The patient was born in Newfoundland and he had spent most of his life in that country. He had the usual childhood infections. He had "rheumatism" fifteen years before, and for several years he had suffered, intermittently, pains in the arms and legs. The joints were not affected. Many years ago in England he suffered a few days of suprapubic pain associated with rectal tenesmus. There were no urinary symptoms at that time. Eight years ago he had lumbago which was marked by pain and stiffness in the lumbar spine, lasting for two or three months. The health of the patient had otherwise been good. He had, however, been chronically constipated.

Eighteen months before admission the patient had la grippe. He was critically ill but did not have pneumonia. After two or three weeks he went to work against the advice of his physician and "caught cold." He then began to complain of increased frequency of urination and urgency and an occasional sense of residual urine. There were no actual dysuria but urination was followed by a sense of marked discomfort in the glans penis. The urine was cloudy but not bloody. There was no difficulty in starting the stream and no lack of bladder control. Bladder lavage was given by the physician, who later suggested the possibility of a recto-vesical fistula when the patient began to pass gas per urethram at the time of voiding. The patient complained also of occasional backache most marked in the left lumbar region. He had, however, regarded that portion of his back as a "weak point" and he had therefore for a long time worn woolen garments because he "caught cold" in his back so easily. Six weeks after the beginning of bladder difficulty, the right testicle became swollen, red, painful and tender. The acute symptoms soon subsided but the swelling persisted for about two months. The urinary difficulties above described continued with occasional periods of relief. After about four months the patient consulted a urologist who, after cystoscopic study, made a diagnosis of chronic colon bacillus infection. He was able to live in comparative comfort but with persistent occasional periods of cloudy urine and gas per urethram, associated with increased frequency. Excessive exercise and exposure to cold weather usually precipitated an attack. He felt otherwise well save for the fact that he became fatigued rather easily. His appetite was good, and he slept well. He stated that he had lost about 10 pounds in the past year and a half, but that this loss had not been progressive.

Examination found a well developed and well nourished, rather obese adult male of advanced years. His appearance was not suggestive of critical illness. Temperature, pulse and respirations: normal. The routine physical examination was not remarkable. The abdomen was adipose and palpation was unsatisfactory. There was no muscle spasm and no masses were felt. The liver edge was barely palpable; the spleen

and kidneys were not palpable. There was slight tenderness in the left costo-vertebral region and definite tenderness on the right side, at the tip of the 12th rib. Urine: cloudy, acid, 1.008, slight trace of albumen, no sugar, many pus cells. Hemoglobin: 90 per cent. White blood count: 13,000. Cystoscopic examination revealed mild cystitis, inactive infection in the left renal pelvis, and an active right pyelitis marked by the presence of pus in the right ureteral specimen and a positive colon bacillus culture on that side.

With this evidence of chronic infection and without demonstrable signs of other pathology, lavage of the right renal pelvis was begun. The patient returned to his home and reported at the hospital frequently for treatment. Under the course of therapy, his condition improved. He reported that his urine was more clear, and that his pneumaturia was less marked although it did not disappear. After several weeks, however, following exposure to cold, he again became extremely uncomfortable. The urine was clouded with pus and gas was passed frequently per urethram. As soon as his condition permitted, a barium enema was ordered, with the interesting result that a few hours later, barium sulphate was passed with the urine. The x-ray plate of the large intestine revealed a lesion of the pelvic portion of the sigmoid. Cystoscopic study of the bladder then revealed in the mid-line posteriorly, near the vault, a small punched-out reddened opening.

With a diagnosis of diverticulitis of the large bowel with a vesico-colic fistula, operation was performed. The diverticulitis of the sigmoid was found and the bowel was adherent to the bladder. The two structures were divided and a communicating fistulous tract was revealed.

Diverticulitis of the sigmoid is, in all probability, the direct cause of most vesico-colic fistulae. It is an interesting condition about which, until comparatively recently, little has been known. An excellent review of the subject was published in 1908, by Dr. Telling of Leeds. His work may be found in the London Lancet of March 21, and 28 of that year. A complete discussion of the disease cannot be attempted this evening. The possibility of diverticulitis must be borne in mind, however, in our consideration of all cases of urinary tract infection with pneumaturia.

Dr. J. W. KEEFE: Diverticulitis must be considered as a condition which exists much more frequently than the literature would lead us to believe, and it is a condition to be kept in mind in all cases of persistent pyuria associated with the passage of gas from the urethra.

Dr. A. L. CHUTE: I should like to ask the further fate of the two cases of diverticulitis reported by Dr. Graves.

Dr. GRAVES: I thought I would not take more of your time by discussing these cases beyond the point of diagnosis. In case 1 a considerable area of the sigmoid was involved. In a first stage operation the

fistula was repaired and a colostomy was performed. In a subsequent operation a resection of the affected bowel was accomplished with very satisfactory results. In case 2, a simple repair of the fistula seemed sufficient. It is possible, however, in such a case, that the involved area of intestine may require further surgical treatment at some later date.

Dr. R. F. O'NEIL: I should like to ask what the end result was in the two cases of diverticulitis which Dr. Graves reported.

Dr. J. W. KEEFE: I would also like to have Dr. Graves state what was done after this diagnosis was made.

Dr. GRAVES: The first case that I reported, that of the individual in a very excellent state of health with a history of an excellent tolerance of has infection, was operated on and a diverticulitis of the pelvic portion of the sigmoid was found which apparently had given but little inflammatory reaction. At one point the characteristic hyperplastic reaction had taken place with adhesions to the bladder and a perforation through into the bladder cavity. It did not seem justifiable in that individual to go farther than the separation of the two structures and the closure of the fistula. That was done and the patient made a satisfactory recovery. The last week or so of the convalescence was complicated by a recurrence of fever and by a slight discomfort in the lower abdomen on the left side. It seems entirely probable that that was due to a flare-up in the area involved in the diverticulitis. It also seems certain that at some time in the next few months that patient must undergo further operative treatment for resection of that portion of the bowel. We can give him no assurance that that will not repeat its pathology. The condition was so benign at the first operation that that course did not seem justifiable.

The second case presented a different picture. The individual was in a much poorer condition. The inflammatory process in the sigmoid had gone on to tumor reaction, and that individual was given a two-stage operation, first a cecostomy and then a resection of the sigmoid. He made a satisfactory recovery. His wounds have been entirely closed, and his present condition is satisfactory.

Dr. W. C. QUINBY: In regard to these two cases reported by Dr. Graves, there are two points which are worth noting. The first is the extreme minuteness of the communication between the intestine and the bladder. In one case this was so small that I cystoscoped the patient twice before discovering the fistulous opening. Of course the presence of a large amount of infection also increased the difficulty in accurately observing the hole. This was, as I say, very minute and bore no similarity whatever to those cases in which a fistula occurs between the intestine and bladder as a result of malignancy.

The second point is that in neither of these patients was there any history of an inflammatory process on the left side of the abdomen, a history which we know is common in many cases of diverticulitis. It is hard for me to understand in the absence of this history what the pathological process is which underlies the formation of a fistulous tract between the intestine, and so stout walled a structure as the bladder.

Dr. Graves has discussed the treatment of these cases so that I will not speak of this except to note that it is found from the literature that a considerable percentage of cases of diverticulitis subsequently become malignant. This, of course, is a strong argument for resection of the bowel.

Dr. KEEFE: Many cases are thought to be carcinoma and some cases reported cured by resection may have been cases of diverticulitis. It would seem that they must be more common than we were led to believe formerly. I have seen three cases of diverticulitis of the pelvic colon and I am sorry that I have not some X-ray plates that were taken of a physician who died probably of a perforation of a diverticulum in his transverse colon. But these plates show that diverticula while they are most common in the pelvic colon, may be found in the ascending, transverse and descending colon. This plate must show as many as eighty diverticula in as many portions of the colon. And I was interested to hear Dr. Graves say he was able to recover the barium in the bladder. In this case we used the barium enema and we had some very good plates which showed diverticula plainly. It may be you had only a few diverticula. I suppose it is possible to have only a single one, but in this case the plates showed very plainly indeed so that it would seem to me as being one important method of diagnosing diverticulitis by giving a barium enema. This man was about 40 years old, he had pain and discomfort in his left side and finally an abscess which I opened and drained. It had the fecal odor that you find in cases of appendicitis. I had seen some cases at the Mayo clinic, one in particular that Dr. Wilson, the pathologist, had demonstrated. As a matter of fact, after Dr. Mayo made his resection of the bowel he thought it was cancer, but the pathologist found it was diverticulitis. In my own case the condition proved to be diverticulitis. He made a recovery after draining the wound, but he subsequently had more pain and discomfort, and on one occasion he reported to me that he was passing gas through the urethra and this continued for some two or three weeks when he was willing to have something done in the way of an operation. I had advised him to have a resection of his pelvic colon before he had had this gas coming from the urethra. I operated and separated the bowel from the bladder, but he had a mass there as large as your fist and a great many adhesions of the ileum down to this mass. It was a very difficult operation. I succeeded in closing the opening in the bladder and resected his sigmoid but had to remove so much that I could not make an anastomosis. The diverticula were over such a large extent of the colon. So I made a fistulous opening.

He made a recovery. This was done some six or eight years ago. He is living and able to attend to his business although he has a fecal fistula.

Dr. A. L. CHUTE: When it comes to operation, we have two conditions to meet in these cases of diverticulitis of the sigmoid that have opened into the bladder; in one type, such as the one Dr. Graves reports, there is a little tube-like communication between the sigmoid and the bladder; this is relatively easy to remedy—in the other type, the diverticulum opens into an abscess cavity which in time breaks down into the bladder. This is a much more difficult condition to remedy.

In connection with this I think Dr. Binney will remember a case which we saw with the late Dr. Maurice Richardson and in which he found starch grains and vegetable fibers on staining the urinary sediment. This patient was operated on twice and finally developed acute general peritonitis and died. This was a case in which there was an abscess cavity that opened on the one side into the bladder, on the other side, into the diverticulum.

I reported at the recent meeting of the New England Surgical Society two other cases of diverticulitis of the sigmoid upon which I operated. The first of these, seen some years ago, I lost; the more recent one made a slow but satisfactory recovery.

I feel sure that the thickening of the sigmoid which one occasionally sees with multiple diverticula is often mistaken for carcinoma. In 1913 I saw a man of seventy-four who had symptoms that it was supposed might be due to an obstructing prostate. On examination I found what I felt sure was a carcinoma of the rectum—another consultant concurred in that diagnosis and we advised palliative measures. In 1919, six years later, this gentleman came into my office quite free of his former symptoms and was desirous that since my advice had been [so good before that I operate upon a hernia that was annoying him. I believe the outcome warrants the assumption that this man had a thickened intestine due to a multiple diverticula of the sigmoid and that he did not have carcinoma.

Dr. H. BINNEY: I recall another case which did not have bladder symptoms but had obstruction. A colostomy was done, believing it to be cancer; but it turned out to be diverticulitis. The patient had no further trouble and is still going around with an artificial anus.

Dr. R. F. O'NEIL: I remember cytoscopying a patient at the hospital. He had a great deal of cystitis. I was lucky to find the patient when there was a stream issuing into his bladder; and I think if I had not seen that, it might have been easy to mistake the fistula for a bladder growth or perhaps an inflammatory process.

A Modification of the Bucknell Operation for Peno-scrotal Angle Hypospadias. E. GRANVILLE CRABTREE, Boston. From the Massachusetts General Hospital.

Numerous plastic operations for the construction of considerable portions of the male urethra have been devised. In most of these a constant cause of difficulty has been the serious trouble experienced in making the junction between the constructed urethra and the normal short channel. Ordinarily two or more attempts at closure must be made before success is attained.

Bucknell¹ has, in his operation, recognized the value of a tube constructed in continuity with the normal channel. This is accomplished by making use of scrotal skin turned forward toward the end of the penis with the hinge at the site of the old meatus.

His procedure has been to free laterally flaps of skin from the shaft of the penis leaving a longitudinal strip of skin on the shaft of the penis to serve as the roof of the new urethra. Parallel incisions are made in the scrotal skin and the penis sutured down to the scrotum with a catheter in the new urethra. The penis is left sutured to the scrotum for twenty-one days after which the skin flap so acquired is dissected free and serves to form the floor of the new urethra and its raw surface is closed over by lateral skin flaps from the shaft.

Practically there are objections to the operation.

1. The second stage of the operation is performed in the presence of a considerable degree of sepsis. Part of the sutures are lost.

2. In adults it is difficult to control erections, which are disastrous to plastic operations, for so long as three weeks, while the penis is adherent to the scrotum.

3. An inlying catheter through a plastic lessens the chance of success, on account of inevitable sepsis.

Although recognizing that a long narrow skin flap supported by a narrow pedicle is made in disregard of all the rules for skin grafting in most portions of the body, yet recognizing the unusual vitality of scrotal skin I have performed an operation similar to Bucknell's but all in one stage. This operation seems to me to still further lessen chances of failure by ensuring primary union of the suture lines, avoiding the inlying catheter drainage, and in adults lessening the periods of danger to the graft from erections by shortening the convalescence.

Parallel incisions are made along the shaft of the penis from the tip to the level of the posterior margin of the meatus. These incisions are extended laterally along the coronal sulcus and flaps of skin dissected outwards. This leaves a longitudinal strip of skin $\frac{1}{4}$ inch wide still adherent to the shaft. This strip of skin is the roof of the new urethra.

Below the level of the meatus the parallel incisions are extended obliquely outwards on the scrotal skin to give an increased width to

¹ Bucknell, *Lancet*, September 29, 1907, p. 887.

the scrotal skin flap then continued on the scrotal skin to a distance slightly more than equal to that from the meatus to the tip of the penis. This extra length of scrotal skin allows slack in the skin flap. The parallel incisions on the scrotum are connected by a transverse incision. Beginning at the part farthest from the meatus the scrotal skin is dissected free from the scrotum and brought forward with the

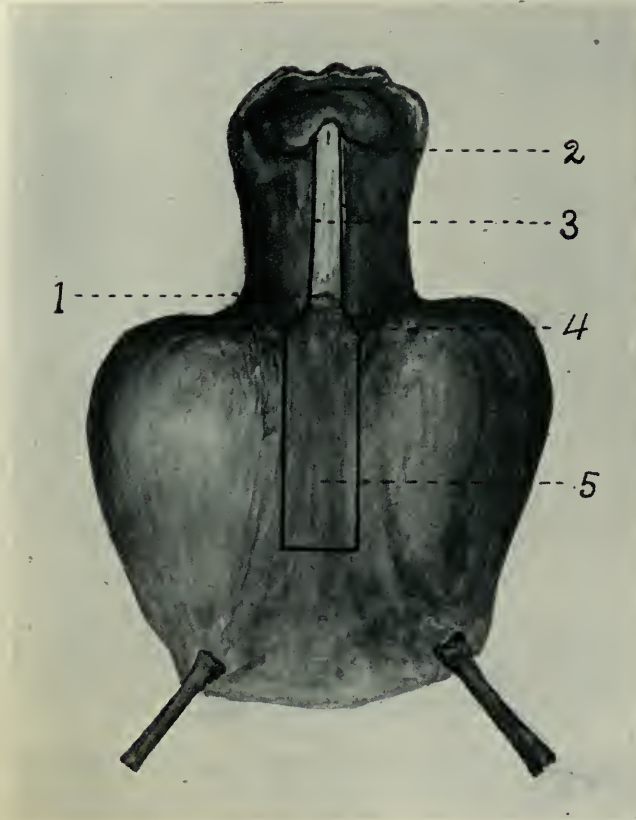


FIG. 1. 1, Meatus; 2, curved lateral incisions along margin of glans; 3, parallel incisions along shaft; 4, shoulder just posterior to meatus; 5, demarcation of scrotal skin flap.

meatus as a hinge and its edges sutured to the strip of skin remaining on the shaft with continuous chromic catgut suture. The lateral flaps of skin from the shaft of the penis are loosely approximated across the new urethra without tension. Sufficient undercutting of flaps should be done to ensure that the sutures are not put in under tension.

In order to avoid inlying catheters I establish perineal drainage at the beginning of the operation. This is easily established without appreciable drainage to the bulb by a simple procedure which I believe to be original with Dr. Richard O'Neil. A small curved hemostat is passed down the urethra to the desired point in the bulbous urethra.

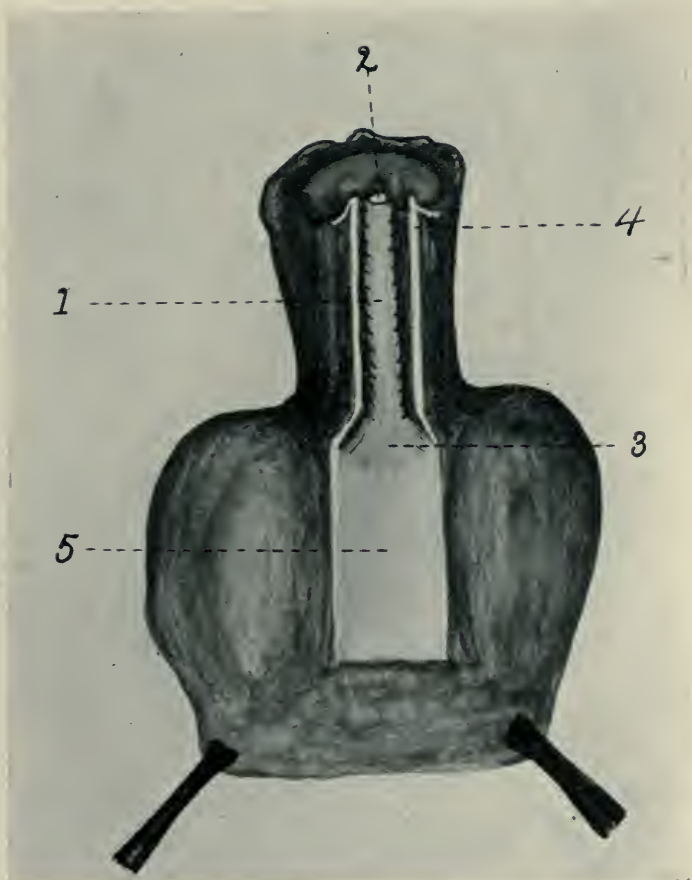


FIG. 2. 1, New urethral tube; 2, new meatus; 3, hinge of scrotal skin flap; 4, lateral flaps reflected from shaft; 5, denuded area on scrotum.

The point is then turned outwards so as to press upon the perineum, the tissues over the point nicked with a scalpel and the instrument pushed through the skin. The tip of a catheter is placed between the jaws of the hemostat and when the instrument is withdrawn it carries the catheter into the urethra from where it can be pushed on into the bladder.

Perineal drainage is continued for two weeks. At this time the tube is withdrawn and the urine resumes its proper channel within a day or two. In the five cases in which this operation has been performed the plastic has healed by first intention in spite of leakage

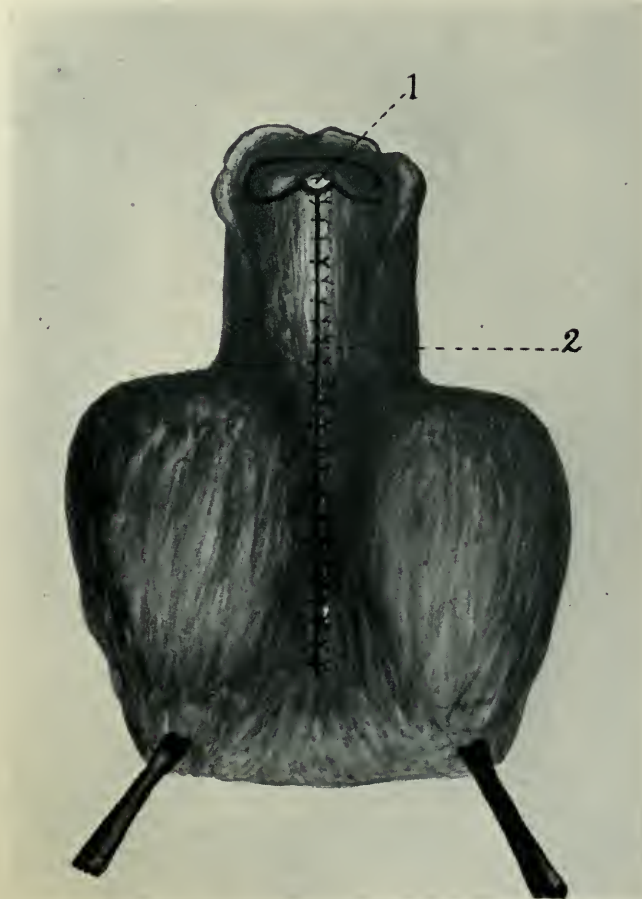


FIG. 3. 1, New meatus; 2, final single line of skin sutures.

through the new urethra, which occurred in two of the cases, on several occasions during the convalescence.

Where cross cutting is indicated for congenital curvature of the penis it should be done previous to the plastic operation and there should be at least two months interval before the plastic operation is done.

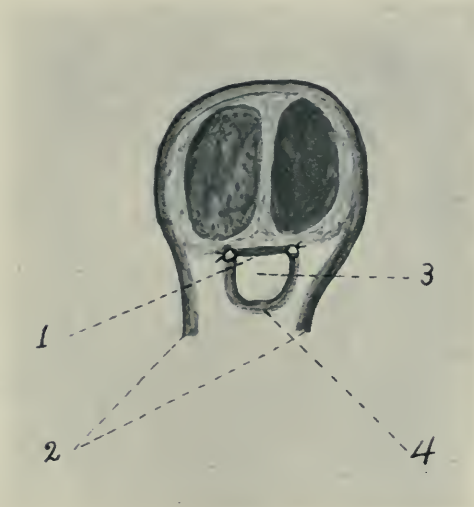


FIG. 4. 1, Strip of skin remaining on shaft; 2, lateral flaps of skin freed from shaft; 3, lumen of new urethra; 4, flap of scrotal skin.



FIG. 5. 1, Strip of skin remaining on shaft; 2, flap of scrotal skin; 3, lumen of new urethra; 4, lateral flaps of skin from shaft; 5, buried cat gut suture; 6, skin closure suture.

Dr. J. H. CUNNINGHAM: I should like to ask Dr. Crabtree if this was traumatic in origin.

Dr. CRABTREE: Yes. It was an attempt to free the floor of the urethra. The floor of the urethra was split clear down to the penoscrotal angle.

Dr. CUNNINGHAM: So that he did not have the usual curving down of the penis?

Dr. CRABTREE: He had some of it but not enough to warrant cross cutting. It seemed to be fairly erect.

Dr. R. F. O'NEIL: In the cross cutting of the fibres would you cut them laterally? This band in the middle makes no difference in the freeing up of the penis?

Dr. CRABTREE: In all except in these two adult cases I have done the cross cutting as a separate operation.

A Study of the Mortality for One Year in the Genito-Urinary Service of the Massachusetts General Hospital. J. DELLINGER BARNEY, Massachusetts General Hospital.

It is always worth while to take account of stock and check up one's work. While we like to know of our successes it is equally important and often quite as instructive to analyze one's failures.

With this idea in mind I have made a survey of the deaths in the genito-urinary service at the Massachusetts General Hospital for the twelve months between October 1, 1919 and October 1, 1920, hoping that by so doing certain errors of judgment or of technic might be avoided in the future.

During the year in question we had 186 admissions and performed 214 operations. Sixteen patients died either within forty-eight hours after operation or while in the hospital, a mortality of 7.4 per cent. We have been fortunate enough to obtain an autopsy in nine of these.

In analyzing this group the writer found himself obliged to undertake the difficult, if not impossible task of looking through both ends of the telescope at the same moment, and if he has erred in his estimate of the situation is it because of this awkward position.

To offset this, so far as possible, the writer has asked each of his colleagues who were on service during the year to express his own views of his own mortality, for there are often many points about a case which cannot be or are not put into the record and which frequently throw an entirely different light on a case.

After very careful perusal of the records, aided by the memory of certain cases, it became obvious that these deaths might be roughly divided into three groups, namely unavoidable, errors of omission and

errors of commission. It also was found that several cases could fairly be placed in more than one group.

Under the first heading I have placed nine cases, unavoidable so far as it is possible to judge, unless one were to argue that they should not have been operated on at all. The futility of such an argument is obvious.

Among these nine cases there were three of stricture of the urethra. One was a man of fifty-five with a filiform stricture of the bulbous urethra. He looked well but had a non-protein nitrogen of 191 mgm. before operation. External urethrotomy was done under spinal novocain anesthesia. There was no untoward reaction. Five days after operation in spite of good drainage and a large fluid intake the non-protein nitrogen was 190 mgm. The daily urine rose from 40 to 150 ounces, being as high as 190 ounces two days before death which occurred nineteen days after operation. Toward the end coma intervened. There was no autopsy. It does not seem as if anything could have been done to avert this death. The kidney damage was unusually severe, although as a mere filter of liquids the kidneys showed marked activity.

The second case was a feeble old man of sixty-five who had been subjected to much rough and unskilled instrumentation before coming into the hospital. There was complete retention of urine with extensive cellulitis of the penis, scrotum and perineum. Under spinal anesthesia (two tablets of apothecin) external urethrotomy was performed, together with multiple incisions of the infected and gangrenous adjacent tissue. The operation was borne poorly. The non-protein nitrogen was 49.8 mgm. three days after operation and the daily output of urine between 70 and 80 ounces. Normal saline was given subpectorally once. Despite all effort to improve his condition the man gradually failed and died on the sixth day after operation. Autopsy showed gangrene of the urethra and scrotum; cystitis; acute ulcers of the stomach; hemorrhage into the stomach and intestines; anemia; chronic pleuritis; edema of the lower lobes of the lungs; arteriosclerosis; hypertrophy and dilatation of the heart. This was an apparently unavoidable death in a feeble, septic old man with chronic renal insufficiency and no resistance whatever. It is possible that more frequent administration of subpectoral salt solution would have turned the scales, but on the other hand it might have overloaded an already dilated heart.

The third patient was a man of sixty-three who had had diabetes for ten years and multiple strictures of long standing. Clinically he presented a picture of marked renal insufficiency with cachexia and a dry red tongue. External urethrotomy was done under spinal anesthesia, tablet "C" novocain being used. Every effort was made after operation to increase the renal excretion and decrease the marked toxemia. The daily urine rose to as much as 180 ounces at times. In spite of a non-proteid nitrogen test of 38.4 mgm., the phenolsulphonephthalein test was only about 10 per cent in two hours, with an appearance time of

thirty-five minutes on the eighth day after operation. The patient died on the ninth day delirious and in coma. He was seen by Dr. R. H. Fitz who excluded the possibility of diabetic acidosis. No autopsy was obtained. This was an urgent operation on a feeble old man with acute retention added to chronic retention, diabetes, low urinary output and no resistance.

There were four patients with obstructing prostate of the benign adenomatous type. The first was that of a feeble man of seventy-two, who survived his first stage, and later his second stage suprapubic operation, only to end up with a secondary hemorrhage from the prostatic cavity on the seventh day after prostatectomy. The bleeding was quickly and completely controlled by the insertion of a Hagner bag, primary ether being administered. Shortly after this procedure the temperature rose, parotitis developed and a blood culture showed streptococci. Death occurred thirty-five days later from septicemia and terminal broncho-pneumonia. Autopsy showed abscess of the lung; chronic pleuritis; arteriosclerosis; hypertrophy and dilatation of the heart; soft hyperplastic spleen; cyst of the kidneys; streptococcus septicemia. This was a personal case and I did not see at the time, nor have I thought since that the death could have been averted.

Another case of obstructing prostate complicated with vesical calculi had a suprapubic cystotomy under local novocain, anesthesia, the stones being easily removed at this time. All went well for fifteen days after operation, when the patient suddenly died of an acute internal hemorrhage. This was found at autopsy to be from a duodenal ulcer, a lesion which had been suspected by our medical brethren in whose ward the patient had been under observation. He was uremic, had more or less complete retention of urine, and thorough drainage of his urinary tract seemed to be imperative. He had two blood transfusions after this operation and his general condition was slowly but steadily improving. It is not believed that cystotomy influenced the onset of internal hemorrhage.

The third case was that of a man of sixty-two in fair condition, but who had had considerable hematuria. Cystotomy from drainage was done under local novocain anesthesia with no evidence of post-operative shock or reaction. Pneumonia developed on the third day and the patient died on the twelfth day after operation. The renal output improves steadily after operation. Apparently an unavoidable respiratory infection in an old man.

Finally there was a man of sixty-nine years with a strongly positive blood Wassermann and a phthalein test appearing in thirty minutes (intravenous) and with only 5 per cent in two hours. The non-proteid nitrogen ranged from 57 mgm. to 33.5 mgm. Cystotomy was done under local novocain anesthesia, drainage continuing for fifteen days, with increasingly satisfactory tests of renal function. Eight days after prostatectomy the temperature rose, the patient became drowsy, the tongue was red and dry and the urine decreased in amount. Sub-pectoral salt solution increased the daily urine to an amount ranging

from 40 to 70 ounces, but produced little effect upon the clinical signs of uremia. The patient died on the nineteenth day after operation of a terminal broncho-pneumonia. There was no autopsy. In view of the onset of renal insufficiency despite long preliminary drainage and increasingly satisfactory tests we were dealing here with a type of case of which I have seen several. All goes well under suitable and sufficiently long preoperative drainage and the standards of safety which we have set up are complied with. Convalescence is satisfactory for a certain length of time, yet in spite of every effort renal insufficiency intervenes, often ending fatally. Were it possible to pick out such a case beforehand a fatality might be avoided by longer preoperative drainage. The case just cited would then come under my heading of errors of omission.

Still another case of obstructing prostate, this time malignant, has been included among the unavoidable deaths. He was a man of sixty-two, in poor condition. He had had two previous suprapubic operations, together with a treatment by radium at a hospital in another city. There was a large suprapubic sinus and a foul bladder and prostatic cavity. Under spinal anesthesia the sinus was enlarged and the bladder explored. Considerable prostatic tissue had been removed either by the knife or by radium, leaving a cavity surrounded by a dense wall of malignant growth. A large suprapubic tube was left in place and the bladder cleaned as well as possible. The patient fared badly after operation dying in forty-eight hours of a terminal broncho-pneumonia. The daily urine was large in amount and there was no evidence of renal insufficiency. It is possible that spinal anesthesia had a share in the fatal outcome—if so it should be considered an error of commission. But in view of marked emphysema and a few scattered râles ether seemed strongly contraindicated and gas oxygen did not appear to be a wise choice.

There was one case of primary cancer of the urethra in a man of sixty-four, interesting because of its extreme rarity. The preoperative diagnosis was stricture of the urethra and periurethral abscess, a mistake often made in these cases. Spinal anesthesia was given. After vain attempts to enter the bladder through the perineum and the excision of a part of the cancerous mass for pathologic examination, suprapubic cystotomy was done. All went well for thirteen days after operation when chest signs developed and the patient died on the twenty-sixth day of bronchopneumonia. Meantime edema of the right thigh, and the condition of the lungs made it clear that we were dealing with metastases in the pelvis and pleural cavity. Unfortunately there was no autopsy.

The last case in my list of unavoidable deaths is that of a man of fifty with renal tuberculosis. Nephrectomy was done without difficulty or complications. Seven days later the temperature rose and from then until his death on the twenty-seventh day the patient steadily failed. On the day of death there was cyanosis, abdominal distension with a board-like belly and tenderness in the left lower

quadrant (nephrectomy was on the right). Autopsy showed small multiple diverticula of the bladder with necrosis and perforation; general fibrino-purulent peritonitis; tuberculosis of the lungs with cavity formation, and chronic pleuritis. The peritonitis may have resulted from the nephrectomy (in which event the case must go under errors of commission) but the autopsy would indicate its origin from a diverticulum of the bladder which had sloughed through into the peritoneal cavity.

Coming now to errors of omission I have placed here two cases with a doubtful third. The latter was a case of stricture of the urethra, already listed as unavoidable. Death was due to renal insufficiency, but it is possible that more active measures, in the form of subpectoral salt solution might have saved the patient.

Of the other two cases one was a patient forty-six years old with calculus pyonephrosis, and certain disturbances of the reflexes suggesting syphilis of the central nervous system. Nephrectomy was difficult as there was a thick, stiffened pedicle. After removal of the kidney a branch of the renal vein slipped out of the clamp with the loss of considerable blood, an unfortunate accident which but few surgeons have escaped. After operation the systolic blood pressure was but 55 mm., this rising to 68 mm. after transfusion, and being 130 mm. two days later. Hemiplegia and aphasia developed and the patient died three days after operation.

Autopsy showed encephalomalacia of the left hemisphere; syphilitic aortitis; ulcer of the duodenum, chronic pleuritis.

It seems unfair to the surgeon to place this case under errors of commission in view of the difficulties of handling the renal pedicle. It seems equally unfair to place it under errors of omission, for although it was recognized that the central nervous system was seriously damaged, the patient was obviously in need of the removal of a badly infected kidney, and it did not seem as if this condition was such as to contraindicate nephrectomy. While there was an unfortunate combination of circumstances in this case, which make its exact classification difficult, I think that in another similar case nephrectomy would be advocated.

The second case was one of multiple diverticula of the bladder with a very bad urine. During preliminary catheter drainage bilateral epididymitis (requiring epididymotomy under ether on one side) and periurethral abscess developed. Suprapubic drainage was then established and continued for twenty-one days with much improvement of the general condition. The non-proteid nitrogen at this time was 32.5 mgm. a figure within normal limits. A phenolsulphonephthalein test might also have been done. Under ether, and after a bloody and difficult operation of three hours duration, a large portion of the bladder base was excised. The patient did quite well for a week, then showed evidences of sepsis and in spite of Carrel tubes and injections he died on the twenty-second day. In summarizing the case the surgeon wrote "In poor shape from severe cystitis due to multiple diverticula.

Drained by cystotomy, later two diverticulum-bearing areas at base of bladder resected. Drainage not adequate. Patient slowly failed and died from sepsis and abscess of the kidney. Perineal drainage would have been better."

Autopsy showed diverticula of the bladder; cystitis with areas of necrosis and disintegration of the bladder wall, with extension of the process into the pericystic and retroperitoneal tissues, with fibrino-purulent localized peritonitis; abscess of the prostate and left epididymis; ureteritis; double pyelitis; right suppurative nephritis; fatty metamorphosis of the liver.

While this case has been classed under errors of omission it might also be included under errors of commission. Although it may have been detrimental to the patient to administer ether for so long a time in the presence of obvious damage to the kidneys, the use of gas-oxygen for three hours would have been difficult if not impossible. Furthermore, owing to the necessity for the Trendelenberg position and the length of time required for the operation spinal anesthesia was out of the question. While it is possible that perineal drainage would have prevented such extensive suppuration the longer time required to open up the perineum would have added another load to the patient's burden.

Under the heading of errors of commission I have placed seven cases, of whom one had already been placed in the unavoidable list and there discussed, and two in the list of errors of omission.

Of the remaining four one was a man of seventy-two with cancer of the prostate. His blood pressure was 195 systolic, 95 diastolic. There was clearly a marked degree of arteriosclerosis. Suprapubic drainage was established with the aid of local novocain anesthesia. Eleven days later, the local and general condition being considered satisfactory, spinal anesthesia was administered. This was done with two and a quarter "C" tablets of novocain. Immediately after this procedure the patient collapsed, developing that curious and characteristic symptom-complex which sometimes follows the administration of spinal anesthesia, a phenomenon seen but rarely now since we know more about the proper dosage. After a time the patient rallied, as is generally the case. It would appear to have been wiser to let well enough alone. Instead of this, but only, it is fair to say, after discussion of the situation with his colleagues, the surgeon continued with the prostatectomy. The gland was found to be cancerous and forty-five minutes was consumed in removing it. There was but little bleeding. The effects of the spinal anesthesia, plus that of the operation were too great for the patient's resistance, and he died within an hour after leaving the operating table. No autopsy could be obtained.

The next case was an obese, apparently healthy woman of thirty-six years with a large vesico-vaginal fistula of over a year's duration. A year before entrance she had had a hysterectomy, and an unsuccessful attempt had been made to repair the fistula. Between the time of her entrance to the hospital in June, 1920, and the following August six operations were performed, the patient being under ether between two

and three hours in all but one of them, and much blood being lost. After the last operation she was badly shocked and died three days later. Autopsy showed focal pneumonia; purulent pleuritis; hypertrophy and dilatation of the heart; soft hyperplastic spleen; cholelithiasis; streptococcus septicemia.

While there is no question that this was a difficult case it seems to be equally clear that there was too frequent a sequence of long and bloody operations.

The third case was a man of sixty-four years, with a benign obstructing prostate and vesical calculi. He was in fair condition and was much improved after suprapubic cystotomy under local anesthesia. Prostatectomy was then performed under spinal anesthesia, this consisting of two and a half tablets of "C" novocain in 2.5 cc. of distilled water, diluted with 2 cc. of spinal fluid, a total volume of 4.5 cc. This was injected into the third lumbar space. In addition to this a small amount of ether was necessary. The patient did well for a few days after operation when the temperature rose, meningeal symptoms developed, and the patient died on the fourteenth day after operation. Autopsy showed purulent meningitis; abscess of the epididymis; cystitis; small miliary abscesses of the kidneys; acute endocarditis; arteriosclerosis; hypertrophy and dilatation of the heart; soft hyperplastic spleen; pneumococcus septicemia.

Coming so shortly after spinal anesthesia the question properly arises whether the meninges were infected at the time of this procedure. So far as is known there was no break in the technic of the administration of the anesthetic. If one can eliminate this possibility the case belongs in the list of unavoidable deaths, otherwise it must go under errors of commission.

Finally there is the case of a woman of fifty-six, well nourished and in good condition, who was admitted with a diagnosis of cancer of the bladder. The growth was near the bladder neck and it had been fulgurated without success on several occasions. Suprapubic cystotomy was performed under ether and the growth which was indurated and ulcerated, and which was found to involve the bladder neck and the region of the right ureter, was cauterized. This was a personal case and although I have a distinct recollection of removing a section of the growth for pathological examination, the pathologist apparently never received it. The small size of the growth, the lack of evidence of metastases, and the patient's excellent condition made the prospects of a successful total cystectomy seem brilliant. As a first step bilateral ureterostomy was done, the proximal ends being brought out into the loins. All went well for eight days when a rise of temperature and faulty drainage from the ureters made it apparent that the operation was not going to succeed. Accordingly bilateral nephrotomy was performed, the tubes being pulled directly into the renal pelvis by means of a clamp which pierced the renal cortex from within outwards. Satisfactory drainage was maintained from both sides for a few days, when the tubes worked themselves out of the kidney. Attempts to replace the tubes through

the cortex and into the renal pelvis met with little or no success, and the urine leaked as much if not more around the tubes than through them. The question of still another operation to replace the tubes properly was discussed but abandoned in the belief that it would be difficult, perhaps impossible, owing to the previous operations and to the considerable obesity of the patient. As time went on grave secondary anemia developed, together with a severe and persistent cough. The temperature remained elevated and the urine which leaked from the two sinuses, became more and more purulent. Death occurred on the seventy-second day after operation. We were fortunate enough to obtain an autopsy. This showed a bilateral pyonephrosis; extensive phlegmon of the retroperitoneal (perirenal) tissues on the left; anemia; ulcer of the duodenum; fatty metamorphosis of the liver. The bladder looked entirely normal and no evidence of cancer either in this organ or elsewhere could be found. Permission could not be obtained for examination of the organs of the chest. In view of the absence of any evidence of cancer at the autopsy the question arises as to whether there was a mistake in diagnosis, the growth being a simple ulceration of unknown origin, or whether the entire cancer was removed by the cautery, curette and knife. Be that as it may the woman's death is pretty definitely due to an error of technic in the performance of both ureterostomy and nephrotomy.

The same methods were employed for both operations which I have found successful in a few other cases of like nature, yet for some reason good results were not attained. Ureterostomy was performed first so that in the event of its failure nephrostomy could still be done, thus giving the patient two chances of success. It is hard to say what procedure I should try in another similar case, but in view of Lower's success with uretero-sigmoidostomy I would certainly consider this operation seriously. All I can say in justification of the failure in these operations is that the patient was very fat, making operations which are difficult even in a thin individual a matter of much greater difficulty and uncertainty.

Having recited in perhaps wearisome detail our fatalities during the year in question one may well ask what has been gained from this review, which will prevent a repetition of the program another year. I wish firstly to emphasize the fact, perfectly well known to all having staff appointments in a large public hospital, that the average patient coming to such a hospital is a much poorer risk than the average patient with similar lesions seen in private practice. Under-nourishment, hard work, an excess of alcohol, uncured venereal disease, neglect or unskilled treatment of the disease for which they are admitted contribute greatly to the difficulties of attaining success. The mortality is, therefore, higher for the most part than obtains in private practice. For the reasons just enumerated one will therefore always be likely to find that a large number of the fatalities in hospital practice will fall into the "unavoidable" column. Secondly the "errors of commission" were those of judgment or of technic. No defence is offered for these

errors except to say that if they are committed by members of a staff which handles exclusively one line of work, and whose every effort is directed toward perfecting themselves in this line, how much more often must such errors be made by one who sees only an occasional case of like nature.

Thirdly I cannot see that any mistake was made in the choice of the anesthetic in any of these cases. In our experience spinal anesthesia is safe and satisfactory. The one patient who died shortly after its administration possibly would not have done so were it not for the operation. Generally speaking, however, one should avoid or be exceedingly careful in the use of spinal anesthesia in those with marked arteriosclerosis and a very high blood pressure. The same caution applies to those with an unusually low blood pressure.

Finally as I look over these cases I feel that while they were given what seemed at the time to be sufficient preliminary drainage and while the fluid intake by mouth and subpectorally both before and after operation was in most cases pushed to the limit of safety, yet I am sure that it is always better to drain too long than too short a time, and to see that the fluid intake is as great as can be borne. I wish also to emphasize the fact that whereas a high non-protein nitrogen figure is not to be disregarded, a figure within normal limits is misleading. The test is valuable, but should always be checked up by the phenolsulphonaphthalein test.

Dr. J. W. KEEFE: It seems to me that Dr. Barney has been very frank in presenting this paper, and it seems to me that papers of this sort do not come before us with sufficient frequency.

Dr. J. H. CUNNINGHAM: I would like to ask what you took for your period of mortality—patients that died in the hospital?

Dr. BARNEY: Yes.

Dr. A. L. CHUTE: I should like to ask what operations were done on cancer of the bladder. Did you do sections or total cystectomy or what?

Dr. BARNEY: We did not do any total cystectomies.

Dr. CHUTE: You spoke of twenty cases of cancer of the bladder with a mortality of 25 per cent. I wondered what the operation was.

Dr. G. G. SMITH: As one of those who contributed his due quota to this lethal list, I should like to say a few words, not in extenuation, because I agree it is a very good thing to be perfectly frank about our results, but in hearing a paper like this, one does not have before his mind the picture of some of the cases in which this fatal result was obtained. Now I remember, for example, the man that had a fatal

duodenal hemorrhage, who had had his bladder opened and vesical calculi removed, because he was one of the cases which I did and he was in perfectly wretched shape when he came into the hospital. I saw him in the office first. I have forgotten what his hemoglobin was but he was lemon yellow. It was thought first that he had a cancer of the prostate. I thought he had a cancer of the prostate at first, but when I examined him his prostate proved to be not malignant and I sent him into the medical side for study. While there, he was obviously getting worse; his bladder was greatly distended and it seemed probable that uremia was largely responsible for his condition. The only thing to do was to transfuse him, open the bladder, remove the stones, and see if he could not get back into shape. This was done, and he really did pretty well, and I think he would have gotten by if it had not been for this hemorrhage from the duodenal ulcer which was not definitely diagnosed. It was believed that he had some malignant condition around the stomach or gall-bladder though the X-rays were negative. He was really a shocking risk though you had to do something for him to give him a fighting chance.

The same thing was true in one of the stricture cases, which came in with a non-protein nitrogen of nearly 200 and a creatinin which the medical men said was lethal—which no man could have and still live. I think his was under five, the lethal point being about five.

I want to say this because in listening to figures which are as shocking as these, one must remember that they come from a general hospital where cases are frequently sent in extremis.

Dr. BARNEY: I have put down under cancer of the bladder "seen 17, with a mortality of 5 per cent." That did not include any total cystectomies but included little bits of things which required a partial cystectomy. We were not so fortunate in the previous years with a mortality of 17 per cent.

Dr. R. F. O'NEIL: I would like to emphasize a point made by Dr. Smith of the very severe cases admitted to the hospital. One case I should like to speak of—pneumococcus meningitis after prostatectomy. This man was in excellent condition, and as I remember it, it was some time after his prostatectomy that he died suddenly. He had had spinal anesthesia but just what the connection was between the spinal anesthesia and the meningitis I do not know. The meningitis should have developed sooner after the spinal puncture, but it might have been an embolic process.

Dr. BARNEY: He died on the fourteenth day after operation but did not do well after the third day.

Dr. O'NEIL: As I remember he did very well and I do not remember any meningeal symptoms at that time.

Dr. BARNEY: It was hard to say when the meningeal symptoms began.

Dr. O'NEIL: That case looked very well, and if it had not been for the meningitis he would have recovered.

Dr. BARNEY: It wouldn't prevent me from giving spinal anesthesia. It did not come soon after the operation.

Dr. O'NEIL: We frequently see on the second or third day that a man has a little fever and discomfort but after salt infusion he is all right.

Dr. BARNEY: I can only emphasize what Dr. Smith has brought out. A paper like this does not give a fair picture. We all know that the hospital cases are bad risks, and some of them are exceedingly bad risks. They are delicately balanced, and the least thing will upset them, and the question of anesthesia does not amount to much. It is not an easy matter to bring that out. Each man should analyze his own cases because there are usually a number of points which he may remember. The fellow that comes from a distance and tries to be impartial cannot bring those points out.

A Case of Apparently Cured Urinary Tuberculosis. GEO. GILBERT SMITH.

In view of the fact that there is no record so far as I know, of any case of renal tuberculosis in which cure has been effected without nephrectomy, either autogenous or surgical, the following case history seems to me of very great interest. It is unfortunate that the evidence does not warrant a hard and fast diagnosis of tuberculosis of the kidney; yet if there was no renal tuberculosis, the case was one of primary tuberculosis of the bladder. In either event, it is worth reporting. I will give the facts in the case and discuss it later. Olga P., age thirty-one, came to the Massachusetts General Hospital Outpatient Department, on November 13, 1914. She gave a history of frequent and burning micturition which had been gradually increasing for the past six months. She was cystoscoped by Dr. Barney. The bladder was not intolerant but held 4 ounces comfortably. Her bladder urine was slightly hazy. Mucosa of the base was red and edematous. The right ureter was dilated and reddened. The catheter would not enter the ureter and no jet was seen to issue from it. The left ureter was edematous, reddened and patulous. A no. 6 catheter passed to the left kidney; at first there was no flow, then a few drops of pale, clear urine. The right kidney was palpable bimanually; it felt rather irregular, somewhat enlarged, and slightly tender. On December 3, 1914, her bladder urine showed many leucocytes and gave a mixed growth of bacteria including the colon bacillus. Urine from the left side showed no pus and no growth. On December 16, 1914, she was cystoscoped

by Dr. O'Neil who found the urine to be cloudy with considerable sediment. The right ureter was dilated, stiffened, and retracted. No jet was seen. A catheter entered for only a short distance and a blue solution injected into the bladder returned through the ureteral catheter. The left ureter seemed normal and gave a normal flow of clear urine. Colon bacilli were grown from bladder and left ureter. Unfortunately the record of the sediment from the left ureter was lost but it is to be noted that the urine appeared normal macroscopically. X-rays showed no stone. It was believed that the case was one of tuberculosis with a dead kidney on the right. The patient entered the hospital for further study. Examination of the lungs showed râles and dullness at the right apex. Then followed a period of study during which a number of guinea-pigs were inoculated from the urine from the left ureter and from the bladder. In all 5 pigs were inoculated. All of them lived their allotted six weeks before being killed. Three of these pigs were inoculated with urine from the left ureter. Of these two showed tuberculous lesions of glands and spleen, and one did not. Two inoculated from the bladder urine showed tuberculous lesions of the glands and spleen. In other words four out of five pigs showed definite tuberculosis. It would seem that such findings could not possibly be due to laboratory tuberculosis in the pigs. The case was discharged from the hospital as one of bilateral renal tuberculosis. This diagnosis cannot be said to have been absolutely established. No urine was ever obtained from the right kidney. There is no record of pus having been found in the urine from the left kidney. In the light of after-thought it would have been wise to have tested the function of the right kidney by the intravenous injection of indigo-carmin. The evidence of bilateral renal tuberculosis, however, seemed clinically strong enough to make it inadvisable to attempt operative interference. She was, therefore, sent to the out-patient department to report to the tuberculin clinic conducted by Dr. J. B. Hawes. Beginning February 10, 1915, she had tuberculin weekly for ten months and then every two weeks for four months; every month for one and a half years and since January, 1918, she has been coming once every month or every two months. In May, 1915, her urine was bloody and she had a frequency of every two hours, day and night. The bladder was treated with gomenol oil instillations. In September, 1915, she began to gain both as to symptoms and weight. By February, 1916, she had gained 28 pounds and had practically no bladder symptoms. On October 22, 1919, she had an attack of frequency and hematuria but this quieted down. In November, 1919, she was married. In December, 1919, her blood pressure taken by an outside physician was said to be 190; when taken in the out-patient department, however, it was only 160. In April, 1920, she returned to the out-patient department and was found to be four to five months pregnant. She complained of some frequency but not more than one might expect as a result of her condition. She was sent into the house for further study and there came under my care.

General examination showed a woman in apparently very good condition. Her lungs showed only a slight dullness at the right apex and no râles. She appeared to be about five months' pregnant. Her urine on May 10, 1920, showed no albumin; no sugar; the sediment showed epithelium and numerous white blood cells. This was not a catheter specimen.

On May 11, 1920, I did a cystoscopic examination. The bladder was clean and held 4 ounces without discomfort. No ulcers were seen. The only abnormality was a band of cicatricial tissue extending upwards from the right ureteral orifice. Both orifices were soft and pliable and apparently normal. Catheters were passed to both kidneys without difficulty and drew clear urine from both sides. Search was made for extra ureteral orifices but none was seen. Phthalein injected intravenously appeared from the left side in four minutes and from the right in six minutes. The density of color appeared to be equal. Less urine was drawn from the right catheter but there was some leakage into the bladder, probably around the right catheter. These urines were put into guinea-pigs; autopsy after six weeks was negative for tuberculosis. The bladder urine was examined for tubercle bacilli and none was found. The patient was in such excellent condition that she was discharged to the Lying-In Hospital for prenatal care. She returned to the out-patient department on June 9, 1920. The urinary specimen showed very little red blood cells, white blood cells, and squamous cells. No tubercle bacilli were found. A guinea-pig was inoculated but died in four days. The urine showed no growth. On September 8 she was taken into the Lying-In Hospital with signs of acute toxemia. Blood pressure arose to 210 and she had general edema. Labor was induced and she was delivered of a 7 lb. child. Although she was badly torn she made a good convalescence, so far as renal function was concerned, and was discharged from the Lying-In Hospital in good condition.

This case is to me very interesting. I do not feel that one can say with certainty that the patient ever had a true renal tuberculosis. There seems to be no doubt but that the left kidney was filtering out tubercle bacilli in 1914 but the absence of pus from the urine on that side prevents one from making a definite diagnosis of renal tuberculosis. The evidence that the right kidney was tuberculous was only presumptive. There is no doubt, however, of the existence of tuberculosis of the bladder. There is nothing to suggest that this tuberculosis was derived from a tuberculous salpingitis and the only other source of tuberculosis would be renal. Either the patient had a renal tuberculosis which is cured or she had a primary tuberculosis of the bladder, the bladder having been infected by tubercle bacilli filtered out through the kidney. It is my belief that in her case the rather remarkable recovery was due to the long continued, intelligent use of tuberculin, aided, of course, by the instruction in hygienic living as given by the tuberculin department.

Dr. A. L. CHUTE: The demonstrated cases of tuberculous kidneys that have recovered with function are so extremely rare that I believe Dr. Smith should bear in mind the possibility that his case had a Y-ureter and two masses of kidney tissue one of which had gone on to destruction with absolute obliteration of the ureter. This seems to me a more probable explanation than that he has a tuberculous kidney that has become cured in the sense that the disease has been stamped out without the destruction of the secreting power of the kidney; the latter condition I believe is one of extreme rarity; to my knowledge there is not a single demonstrated case in which a tuberculous kidney has become cured in the sense that the disease has cleared up and the kidney has functioned practically normally. Some years ago I saw a patient that was supposed to have a cured tuberculous kidney. She had been under treatment for ten years and had no symptoms for some time. She had a sudden hematuria which I found came from her left kidney. I did a nephrectomy removing the remains of a much atrophied tuberculous kidney which had lighted up after a long period of quiescence. The condition is so rare that I believe all reported cases must be gone over with the greatest care and I hope that in this case Dr. Smith will inject the ureter to see if by any chance it is of the Y type and that we have an instance in which an auto-nephrectomy, so called, has taken place in the renal tissues connected with one branch.

Dr. G. G. SMITH: But the tubercle bacilli were obtained from the ureter when it was first catheterized.

Dr. A. L. CHUTE: But with a Y-ureter you would not go up both branches at the same time. In an instance of Y-ureter that I saw some years ago I would get pus on one catheterization and not on another, depending on whether or not I went into the branch of the ureter that was connected with the suppurating pelvis. An injection of thorium made low down showed the ureteral anomaly.

Dr. G. G. SMITH: That is a possible explanation.

Dr. E. G. CRABTREE: I think there have been reported cases in which an abscess which is walled off by caseation is left, and later breaks down and gives pus and tubercle bacilli.

Report of Two Cases of Papilloma of the Renal Pelvis. WM. C. QUINBY.

The first occurred in a man fifty-two years of age who had had no illness of note until about six weeks before entrance to the Peter Bent Brigham Hospital on September 25, 1920. At this time he noticed that the urine contained blood, and this appearance recurred about four days later. Thereafter blood was seen three or four times each week. There were no symptoms whatever on the part of the bladder, such as pain or frequency. Blood pressure was 150/90. The Wassermann reaction was negative. Hemoglobin and white blood count were nor-

mal. The urine was normal except for the fact that it contained numerous red blood cells. The phthalein output was 70 per cent in two hours and ten minutes. General physical examination together with rectal examination was entirely negative.

Cystoscopic examination showed the bladder to be normal, and the left ureter admitted a catheter without obstruction for the usual distance. From this side the flow was normal. On the right side the catheter passed somewhat more difficultly, and from this side there was no flow of urine. Injection of the pelvis on the right side showed it to contain about 19 cc. of bromide solution without producing pain, and examination of the plate thus obtained showed a definite hydro-nephrosis, but the shadow on the plate was very thin, evidently due to the fact that but little of the fluid had penetrated the pelvis. This appearance was not explained until operation, when the true condition of affairs was seen in the fact that the pelvis was found completely filled by papillomatous tissue.

The pathological report of Dr. Wolbach is as follows:

Gross description: Specimen consists of a right kidney which has been opened by median incision. Capsule strips easily. Surface is not remarkable except for several pale projecting cysts, the largest 12 mm. Pelvis is considerably dilated and 7 cm. of ureter is attached. The picture viewed from within is very striking. The main feature is a massive papillary, fungating growth occupying the greater part of the pelvis closely following the epithelium lining of the calices and extending 3 cm. into the ureter, which it practically almost occludes. Many of the calices contain dark red blood clots and at the upper pole the growth is not seen but hemorrhages are seen beneath the mucosa and considerable thinning of the cortex has occurred. The main tumor growth is grossly white with the tips of many of the papillary growths quite vascular and red. The lower part of the pelvis is occupied by the largest growth of tumor, projecting nearly 2 cm. into the pelvic chamber. That lining the calices is more fungiform, forming a rather thick, greyish-white and nodular layer which extends over the entire surface of many calices but does not entirely cover others. Implantations of more recent tumor growths are present in the calices of the upper pole and they vary in appearance from slightly raised plaques 2 to 3 mm. in size to irregular nodular projections 4 to 5 mm. in height. The cortex, after kidney has been fixed in Klotz fluid and formalin for several days, shows considerable irregularity. Glomeruli do not stand out prominently and arteries appear thickened. Cortex and medulla are greyish-white mingled with bright red petechial hemorrhagic areas and there appears to be considerable invasion by connective tissue. In the lower pole just beneath the capsule is a greyish-white tumor growth, rather oval in shape, projecting about 1 mm. above the surface and extending into the cortex about 4 mm. It does not appear encapsulated but is fairly well outlined. It is slightly spongy in consistence and there are numerous small blood vessels visible on the cut surface. It is covered externally by the renal capsule which is

reflected over the surface and seems to be definitely embedded in the cortex.

Microscopic report: A section from the region of the pelvis shows wide, papillomatous outgrowths of transitional epithelium. These are closely packed and in blunt villous projections into the pelvis. At the tips of some of these villi are groups of dilated capillaries, some of which have ruptured into the surface. The villi are supported by a central core of connective tissue in which run a few thin-walled blood vessels. The growth does not extend into the parenchyma of the kidney. Below the basal layer of the growth are seen foci of mononuclears.

The other tumor is composed of thick, branching strands of connective tissue covered by transitional epithelium. These simulate congeries of embryonic tubules, many of which are dilated and contain an albuminous precipitate. Here and there epithelial lined structures contain what appears to be embryonic glomeruli. A scant amount of stroma, containing capillaries, supports these.

Diagnosis: Papilloma of pelvis; papillary adenoma of kidney.

The second case occurred in a man of fifty-two years of age who, except for influenza about a year ago, presented a negative previous history. In August, 1919, the patient began to void dark red urine for no known cause. This has continued intermittently until the present and for the past month the urine has been almost continuously of a deep red color. There have never been any symptoms on the part of the bladder, but recently there has been an occasional pain in the left lumbar region which has often preceded the appearance of blood. On entrance to the Peter Bent Brigham Hospital on the twenty-fifth of September, 1920, the patient was found to be apparently normal in all regards except that there was found to be a double hydrocele. Hemoglobin was 90 per cent; the phthalein output 60 per cent. The Wassermann reaction was negative, and the blood pressure was 140/85. The urine showed a considerable amount of blood and a few leucocytes.

On cystoscopic examination the bladder was normal. On the right side the ureteral catheter delivered normal urine, while on the left the flow was scanty and blood tinged. Examination of the outline of the pelvis after injection showed definite irregularity in the calices of the lower pole suggesting neoplasm. The calices of the upper pole did not contain any of the injected fluid.

The pathological report of this kidney, also made by Dr. Wolbach, is as follows:

Gross description: Specimen consists of a left kidney which has been opened by a median incision. About 5 cm. of ureter is attached and there is considerable pelvic fat. After being in Klotz fluid about two weeks it measures 12 by 4.5 by 5.5 cm. Capsule is stripped. The anterior surface shows no gross abnormality. Faint depressions mark out the six original lobules of the surface. On the posterior surface the capsule is adherent slightly to the upper quadrant, while the cortex is speckled with bright red, slightly projecting nodules giving a very

coarsely granular surface to this more or less well marked out lobe. About 2 cm. from the hilum of the posterior surface a cyst 1 cm. in width projects above the surface. It contains a thin, slightly brownish fluid. It suggests the ordinary retention cyst. Projecting from the lower pole abutting on the hilum is a tumor mass 4 by 3.7 by 1.3 cm. It is firm, yellowish-white with irregular, somewhat lobulated surface. There are numerous bright red, petechial hemorrhages beneath its capsule.

The kidney viewed from within shows a relatively normal appearing cortex which averages 8 mm. in thickness. Glomeruli are of about normal prominence except in the upper pole. This portion shows thinning out of medulla and cortex, due to the presence of a cauliflower, fungating tumor mass arising apparently from the pelvis and filling the upper half of the pelvis. The tumor consists of many papillomatous growths arising from a rather large pedicle and extending toward the cortex away from the hilum. It is a yellowish-white intermingled with small blood clots. In the calices in the anterior wall there is a carpeting of pale, papillomatous tumor tissue which extends almost to the pyramids. Some of these outgrowths are long, narrow and quite villous in appearance. This growth does not appear to invade the kidney proper and stops short of the ureteral orifice. The lower half of the pelvis shows much injection of the mucosa and large, blotchy hemorrhages are quite conspicuous. The tumor mass described on the posterior surface has encroached upon the pelvis considerably and is well encapsulated. It is firm, uniformly orange-yellow, and contains many small blood vessels. It extends from the level of the pelvis to 2 cm. from the capsule of the kidney below. It does not communicate with the pelvis in any portion. Surrounding it is a moderate amount of pelvic fat in addition to the capsule. There is slight flattening of the pyramids below this tumor mass.

Microscopic report: Contiguous with the epithelium of the pelvis are finger-like projections into the pelvis of atypical epithelial cells resembling the transitional or pelvic type. Numerous mitotic figures are found. In one section the tumor cells have invaded the medulla and are surrounded by numerous mononuclear cells and fibroblasts in a few areas. The remainder of the parenchyma has patchy and diffuse scarring throughout its interstitial portion, causing pressure and atrophy of some of the tubules; sclerosis of a few glomeruli, and focal collection of mononuclears. Intimal changes are present in the larger vessels, while the small vessels also show thickening. The other tumor is composed of closely packed cords of epithelial cells with slightly granular though pale cytoplasm separated by vascular interstitial tissue suggesting adrenal cells.

Diagnosis: Papillary carcinoma of pelvis with extension into kidney; hypernephroma; chronic vascular nephritis.

It is evident from this that the bleeding in this case occurred from the papilloma and not from the hypernephroma.

Dr. R. F. O'NEIL: Is the pelvis entirely blocked off in your picture?

Dr. QUINBY: Very little bromide solution got in due to the fact that the pelvis was filled with tumor, but you can see the enlarged calices faintly in the plate, but only in a good light. In the other case the hematuria occurred from the tumor of the pelvis and not from the hypernephroma.

Dr. J. W. KEEFE: How many cases have you seen of papilloma of the kidney?

Dr. QUINBY: These are the only two cases I have seen.

Dr. J. W. KEEFE: How many cases have you seen, Dr. Chute?

Dr. A. L. CHUTE: None.

Dr. R. F. O'NEIL: I recall one case of papilloma up and down the ureter seen at autopsy.

PRIMARY TUBERCULOSIS OF THE BODY OF THE TESTICLE

ERNEST G. MARK

From the Urological Department of the Research Hospital, Kansas City, Missouri

Admittedly, tuberculosis of the body of the testicle as a primary focus in the human economy, is unthinkable. As a primary manifestation of urogenital tuberculous infection such a focus must be considered of the most extreme rarity. That it may occur, at least experimentally is shown by George Walker's work on rabbits. Of 28 rabbits receiving an injection of tubercle bacilli direct into the aorta, 2 showed testicular tuberculosis without epididymal involvement. Critical review of all available literature by all of the latter investigators on the subject finds no substantiated clinical case and we can find no one of the reported instances of primary tuberculosis of the body of the testicle which is not open to serious question. In fact the case which we desire to report here, we believe will bear out this contention.

There is apparently but one case of this character which seems to be generally accepted in the exhaustive references on the subject—the case reported by Gilbert Barling in 1892, but in this instance serial sections were not made and in this case there was also tuberculous disease of the right apex, recognized by physical findings. Reclus in 1876 collected three cases of supposedly primary tuberculous involvement of the body of the testicle and Sommer in 1836 reports a case of double involvement in a man of thirty-six years of age. It seems hardly necessary to state that the dates of these reports with the manner of investigation at that time excludes them from consideration.

Kidd, 1920, says in reference to K. M. Walker's experiments:

Walker attempts to prove that tuberculosis of the testicle does not occur except in the presence of previous tuberculosis in the prostate

gland. I have seen a number of cases where tuberculous lesions have been confined to the testicle alone, and the same can be said of lesions of the testicle caused by the colon bacillus.

The term testicle, as used by Kidd, shows a looseness in differentiation between the body of the testicle and the epididymis, as is evidenced by the latter part of the last paragraph of this quotation. In fact, this looseness of terminology is especially noticeable in all articles on the subject appearing previous to the year 1900. However, this same lack of terminology is noticed in the articles of Murphy and of Young which appeared in 1900-1901 respectively.

Walker and Hawes, 1911, state: "Tuberculosis of the testis is not a pathological entity."

One is tempted to refer briefly to the autopsy findings of Reclus and of Fowler and Goodlea. In 500 autopsies on tuberculous cases (phthisis) Reclus found the genito-urinary tract infected in 12.8 per cent. This infection was confined to the testicle and epididymis in 3.8 per cent. Fowler and Goodlea in 531 cases found involvement of the genito-urinary tract in 5.27 per cent with involvement of the testicle and epididymis in 1.7 per cent. Kocher in 451 autopsies performed on cases of tuberculosis of the genito-urinary tract found 83 per cent of lung involvement. Reclus found in 30 cases of tuberculosis of the genito-urinary organs that pulmonary tuberculosis had been diagnosed in 53 per cent of cases by physical signs. In a similar series that came to autopsy there was found pulmonary involvement in 67 per cent of cases.

The case which we desire to report is as follows:

Research Hospital, Hospital no. 27596.

B. J. G., age thirty-one; married four years; father living and well at sixty-four years; mother living and well at sixty-six years; one brother, age thirty-two years, living and well; one sister, age twenty-nine years, living and well.

Previous history. Ordinary diseases of childhood. Pneumonia six years ago with prompt recovery. Appendectomy in March, 1919; recovery uneventful. General health has been excellent with the above exceptions. Habits good.

Genito-urinary history. Gonorrhea fourteen years ago, complicated by acute left epididymitis; recovery complete in seven weeks. Eight years ago patient was kicked in the right testicle during a football game. No swelling or after effect. In February, 1920, patient noticed a slow enlargement of the left testicle which continued until about March 25, when it became quite tender and the swelling rapidly grew worse until April 3, 1920, when he consulted Dr. Wm. J. Frick, of Kansas City, for the condition, at which time I was called in consultation. There was, at this time, a slight hydrocele. The body of the testicle was markedly involved with a small nodule on the body proper. There was no evidence of any involvement of the epididymis or vas. Rectal examination showed a normal prostate as to size and consistence with both vesicles barely palpable. There was no nodulation.

Physical examination. Patient well nourished; weighs 155 pounds, which has been normal for him for the past two years. Heart, lungs and abdomen negative; glandular system negative, no evidence of disease elsewhere.

Laboratory examination. Urine. Specific gravity 1.010; no blood; no pus; no bacteria; no casts; reaction alkaline; expressed seminal fluid shows active spermatozoa with no pus or organisms; prostatic fluid negative; guinea-pig injection of urine negative after twelve days.

Blood. Hemoglobin 90 per cent; reds, 4,440,000; whites, 9,600; polys, 70 per cent large lymphocytes, 6 per cent; small lymphocytes, 22 per cent; eosinophiles, 2 per cent; coagulation time, two minutes. Radiograph of chest negative for pathology. Wassermann, negative.

Operation. April 6, 1920, revealed a large slightly nodular testis with small hydrocele; epididymis and vas normal in every particular.

Orchidectomy was done. The patient made an uneventful recovery and left the hospital in one week. Specimen sent to laboratory from which came the report of a diffuse tuberculosis of the testicle with no involvement of the epididymis.

It seemed impossible that such a condition could exist and I requested a second report from the laboratory explaining to the pathologist, Dr. Wm. K. Trimble, that the condition as reported by him was not a pathological entity. The report again came back that there was no involvement of the epididymis which report I accepted as final but insisted upon serial sections. This latter report reached my desk a few days ago and is as follows:

"Specimen: Testicle with Epididymis attached.

"Slide No. 2562. Hospital No. 31233.

Specimen weighs 52 gms.

"Examination of the gross section shows the testicle to be slightly nodular over its cortical portion. The tunics covering the testicle are somewhat thickened and show ecchymosis in spots. The epididymis is bound down to the testicle by a loose edematous connective tissue, is rather broad and flattened against it and assumes an S-shape as it extends downwards.

"Gross section of the testicle shows it to be of a uniform, firm homogeneous consistence, and of a pale pinkish gray color. No normal testicular substance can be seen. Sections made of the testicle show a typical diffuse tuberculous process with distinct coalescing tubercles with numerous giant cells but with no distinct areas of caseation. Tubercle bacilli were found in sections stained with carbol-fuchsin.

"Serial sections of the epididymis show normal epididymal tubules throughout surrounded by loose edematous tunics except for its extreme tip which shows a small irregular fibrous nodule. Sections of this nodule show a small single tubercle about 4 mm. in diameter which differs in no respect from those found in the testicle. Giant cells are quite numerous but little or no caseation is present. There is a slight irregular fibrosis surrounding this tubercle. Sections of the remaining portions of the epididymis show the tubules to be practically normal but the connective tissue surrounding the tubules is edematous with a slight mononuclear cell infiltration.

"From the appearance of the lesions in the testicle and epididymis one is not able to say with certainty which may be the older. Histologically, the processes in both are identical."

At the time of receiving the second report we sent out forty-six questionnaires to leading urologists in the United States and received thirty-two replies, all negative. Dr. Irwin Abell of Louisville, Ky. returned the following report:

Years ago, about 1906, I operated on a mulatto at clinic, removing what was clinically a tuberculous testicle; the body presented typical naked eye appearance of caseation, infiltration and "cold" abscess formation. As you know, in those days, no microscope examination was made, consequently I have never felt that such diagnosis could be accepted. No further evidence of disease of any type was found.

In the answers to some of the questionnaires, reference was made to reports in the literature which had impressed the readers of such reports as being evidential of primary tuberculosis of the

body of the testis. All of these reports were reviewed by us and the conclusion was reached, as stated in the first part of this paper, that clinically, primary tuberculosis of the testis does not exist. Certainly, the report of cases can not be accepted as such, due to lack of proper investigation as is borne out by the case which we here report with two negative findings of tuberculous involvement of the epididymis by an excellent and careful pathologist, who later reported from serial sections involvement of the epididymis.

It is not within the province of this paper to discuss in detail the various experimental work of Baumgarten and Kraemer, Paladino-Balndini, George Walker, Teutschlander, Oppenheim and Low and others, which work however, has been carefully reviewed. After this review we have come to the conclusion that in the vast majority of cases, primary tuberculous involvement of the genital tract is an ascending process. If such may be accepted as a priori reasoning or if the excretory theory of Belfield, which theory has many exponents, may be accepted the case here reported may be considered one of primary tuberculosis of the body of the testis. If not, then all reported cases of primary testicular involvement must be open to most serious question.

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A STUDY OF TUMORS OF THE VESICAL NECK AND THE PROSTATIC URETHRA AND THEIR RELATION TO THE TREATMENT OF CHRONIC PROSTATITIS

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In a previous paper (1) stress was laid upon the fact that there is often persistent reappearance of pus in the prostatic and vesicular secretions with ordinary routine treatment in cases of chronic infection of the lower urogenital tract. In some instances a more thorough study of these cases revealed the presence of inflammatory tumors which by constant irritation caused a recurrence of the infection in the prostate and seminal vesicles. Briggs (2), in 1889, reported a case of chronic recurrent urethritis which he finally relieved after recognizing and removing through the endoscope, a raspberry shaped tumor of the verumontanum. Neuberger (3) reported persistent cases of chronic gonorrheal urethritis that were finally cleared up by the removal of infected polypi. Klotz (4), Uteau (5) and Lydston (6) report cases in which chronic urethritis in males was cleared up after the destruction of polypi in the urethra. Gouveau (7) reports one, and Morrow (8) three, cases of chronic prostatitis and seminal vesiculitis which resisted the routine form of treatment and were relieved after the removal of urethral polypi. Since the introduction of the endoscope by Desormeaux (9), these tumors have been described by different observers. Tarnowsky (10) described the endoscopic appearance of these tumors in the living subject. Luys (11) calls attention to their frequency in the prostatic urethra and the bladder neck. Walbarst (12) in 1914 made a series of photographs of wax models of these lesions. There is no doubt that many of these tumors were frequently overlooked by the use of the ordinary endoscope, as pointed out by Town-

send and Valentine (13), and by Buerger (14). This difficulty can be overcome by the use of the cysto-urethroscope. With water dilatations slight irregularities and small polypoid and papillary growths which become flat when exposed to the open air can readily be detected.

SYMPTOMATOLOGY

In the past three years the sixty-eight cases presented in this article were collected. All of these tumors were seen in the posterior urethra or vesical neck. In table 1, the symptoms occurring in these cases are given in their order of frequency.

TABLE 1
Frequency of symptoms

SYMPTOMS	CASES
Pain and discomfort in the perineum	57
Constant or repeated morning drop	54
Dull lumbo-sacral pain "backache"	52
Pain or sensation of itching at or inside the meatus	51
Inguinal pain	20
Hypogastric pain	13
Increased frequency of urination and tenesmus	10
Diminution of the sexual power	10
Pain in the testes	9
Premature and painful ejaculation	8
Sensation of a mass lying in the urethra	3
Terminal hematuria	1
Ball-valve interference of the urinary stream	1

The frequency of the occurrence of these tumors in the past has usually been underestimated. However, Oberländer (15) believed that tumors of the male urethra occurred as frequently as caruncles and blood vessel tumors of the female urethra and that the diagnosis was often missed because of the lack of proper endoscopic research. They have been observed in varying frequency by different men. Probably the highest estimate is that of Elder (16), who reports three polypi and seven papillomata in one hundred cystoscopies. Pelouze (17) reported fifty-one cases of lymphoid and cystic bodies in the urethra in thirty-five hundred cystoscopies. All of these cases were of a tuberculous type first described by him.

DIAGNOSIS

The accurate diagnosis of these tumors can be determined by the use of the cysto-urethroscope under water dilatation although their presence can often be suspected by the chain of symptoms peculiar to these lesions and by the persistent reappearance of pus in the prostatic and the vesicular secretions.

A complete urine analysis, including Gram-stain and acid fast stain for organisms, was made in all cases. Guinea-pig inoculations for tuberculosis were also uniformly made. Other foci, i.e., pyelitis, cystitis and prostatic calculi, were ruled out. It is interesting to note that in none of the sixty-eight cases here presented was tuberculosis of the urinary tract demonstrated. However, in a number of cases of tuberculosis of the urogenital tract, the lymphoid and cystic bodies in the urethra, so well described by Pelouze, were seen.

A review of the histology of the posterior urethra, bladder neck and trigone shows the presence of numerous glands. Testut's (18) description indicates that they are indentations of the transitional epithelium more or less developed. They may be either simple cylindrical, or multilobular and extend through the thickness of the sub-mucosa, or are single crypts of the mucosa itself. They do not themselves secrete mucus, but the secretion, if any, is made up of the desquamated epithelium of the superficial layers. Piersol (19) describes two types of glands using the terms intra-mucous and sub-mucous according to their location in the mucosa. Griffiths (20), in describing the middle lobe of the prostate, states that there are ducts opening on the posterior wall of the prostatic urethra between the vesical neck and verumontanum. These ducts are short, mere channels in the stroma, destitute of any special coat except the epithelium lining them. Lowsley (21) later describes a number of tubular structures which are contained within the muscular walls of the prostatic urethra and considers them to be glands of Littré. They differ from the prostatic ducts in that they are smaller, have fewer branches, and lack a muscular coat.

One can readily see that in the presence of infection these glands may undergo inflammatory changes, increase in size,

and project and encroach upon the lumen of the prostatic urethra or vesical neck. The ducts often become occluded and act as a site of retention of infection, which, in turn irritates and prolongs the pathological condition in the prostate and seminal vesicles.

The macroscopic appearance of these tumors is accurately determined with the cysto-urethroscope under water dilatation. We observed the three following types:

1. The true polypus, the base of which is pedunculated.
2. The polypoid mass, the base of which is sessile.
3. A simple edematous excrescence of the bladder neck or the urethral wall.

TABLE 2
Location of tumors

TYPE	NUMBER OBSERVED	POSITION		
		Vesical neck	Prostatic urethra	Bulbous urethra
Polypus	37	12	23	2
Polypoid mass	26	11	15	0
Edematous excrescence	5	3	2	0
Total	68	26	40	2

Careful microscopic study of these lesions confirmed the findings of Randall (22), who, in 1913, under the common name of polyp included all benign tumors of the male urethra. He subdivides these polypi into three groups: (1) Pure or benign fibrous polyp, (2) Villous or papillomatous type or benign villous polyp, (3) Glandular type or benign glandular polyp. In all the three groups he calls attention to the presence of a general round cell infiltration throughout the growth, associated with chronic granulation tissue due to a focus of infection which is long continued.

CLASSIFICATION

Great confusion exists in the literature in this regard. In some instances, authors have based their findings on the microscopic, others on the gross appearance. Owing to the ease with

which caruncles can be observed in women, they were often described with and considered a type of polypus. Linhart (23) describes caruncles as scarcely distinguishable from polypi and condylomata. Williamson and Attlie (24) observed two types of caruncles, the granulomatous and those which are new growths with glandular tissue and proliferation of the epithelium. Lange (25) reports fifty-eight specimens of caruncles, nineteen granulomata due to infection, and thirty-nine true new growths, some of which are glandular. A large papilloma of the posterior urethra was observed by Marion (26) in removing the neck of the bladder in a young adult who had complete retention of urine. Mark (27) calls attention to the confusion between papillomata and polypi. Winckel (28) considers condylomata to be poorly vascularised papillomata. Garodistsch (29) described two polypoid infiltrations of the male urethra as being made up of infiltrative granulative tissue. In 1913, Randall (22), after a careful review of the literature accepted the view of Burkhardt (30), that the term caruncle be limited to lesions in the female. He advocates eliminating condylomata as a type of urethral tumor and under the general term of polyp describes the fibrous, villous and the glandular types. With the cystourethroscope, we have classified these urethral tumors in the male into three types according to their morphological appearance: (1) The true polypus with a pedunculated base, (2) the polypoid mass with a sessile base, (3) the simple edematous excrescence of the bladder neck or the posterior urethra.

PATHOLOGY

Histologically the polypus or the polypoid mass may be either glandular or fibrous. In this series of cases the villous type of glandular polypus was not observed. The simple edematous excrescence of the urethral wall and bladder neck is probably an early result of inflammation of the mucosa and sub-mucosa including the mucous glands. As the inflammatory process advances, the simple excrescence develops through the stage of polypoid mass, later to become a true polypus with a pedunculated base. Pathological descriptions of these tumors may be found with the case reports.

CASE REPORTS

Case I. J. R. Male. Age forty-three. Occupation: Street paver. Out-patient department no. 55867.

Family history: One uncle died of tuberculosis at the age of twenty-five. There was no co-residence. Past history: Malaria, heart

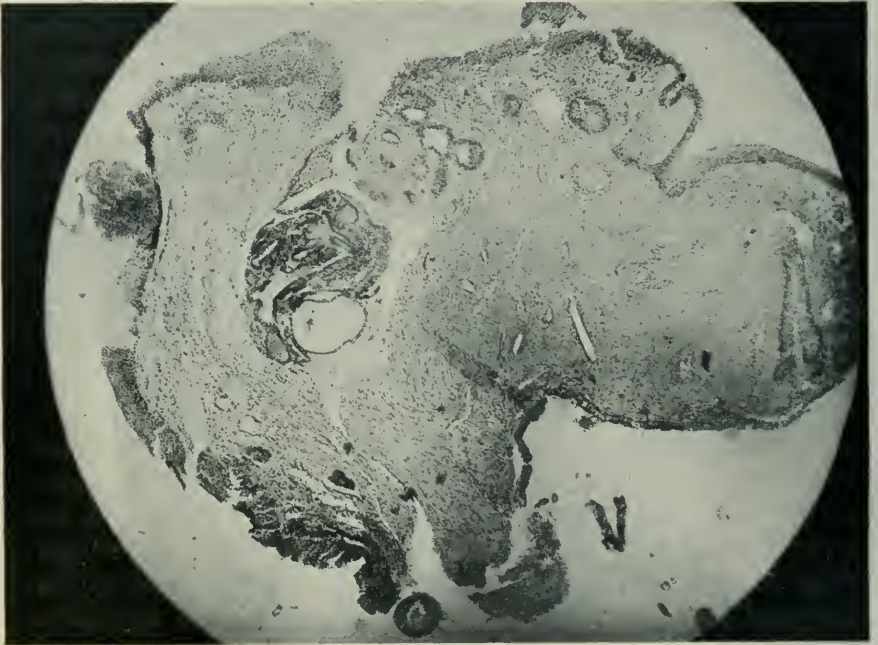


FIG. 1. SMALL GLANDULAR POLYPUS SHOWING A SUBACUTE INFLAMMATORY REACTION. CASE I
Leitz oc. I, obj. 3

disease, and arthritis left shoulder. Fourteen years previously gonorrhea, which was treated by a doctor and apparently cleared up in six weeks without any complications. For the past thirteen years his sexual power has gradually diminished. There is premature ejaculation and nocturnal emissions. There is more or less continual morning drop and discharge on straining at stool. He has a constant, dull, lumbosacral pain which is accentuated on bending the body. There is a sensation of itching and discomfort in the meatus on voiding, and

discomfort in the perineum. The urine shows shreds in the first and third glasses, and is negative on microscopic study, culture, and inoculation of guinea pigs for tuberculosis. The lower uro-genital tract shows bilateral seminal vesiculitis and prostatitis. The lungs are negative. The blood Wassermann is negative. With the cysto-

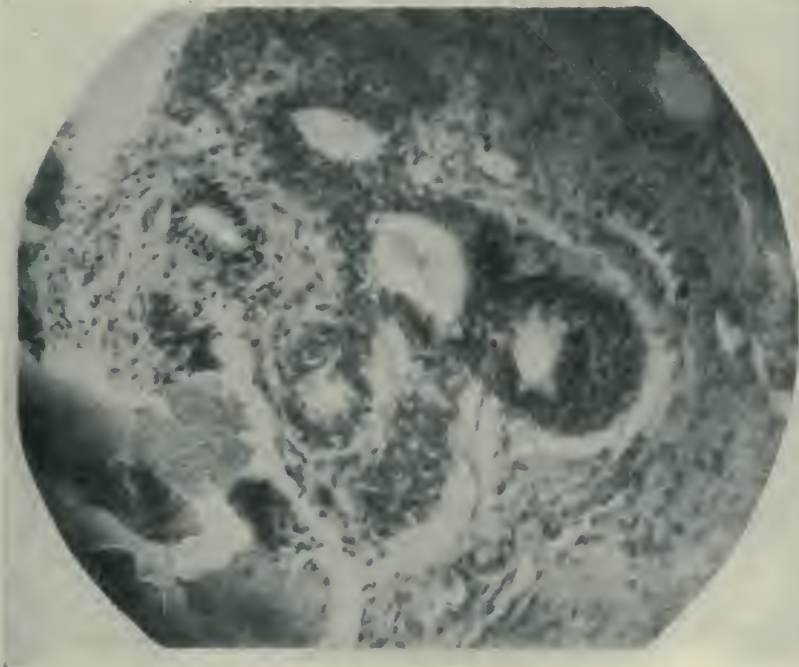


FIG. 2. SMALL GLANDULAR POLYPUS SHOWING A SUBACUTE INFLAMMATORY REACTION. CASE I
Leitz oc. I, obj. 6

urethroscope a large pedunculated, irregular, hyperemic polyp, the base of which was attached to the verumontanum was observed.

Pathological report: Microscopic sections show an irregular mass of tissue which is covered on all sides by transitional epithelium. (The sections were apparently taken transversely and parallel to the base of the polypus.) The surface has an irregular contour but is not papillary in type. The epithelium is thickened at certain points, and shows an invasion of a few polymorphonuclear leucocytes. Beneath the epithe-

lium there is a zone of loose, edematous, reticular connective tissue which shows a rather marked diffuse infiltration of lymphocytes, with a few polymorphonuclear leucocytes scattered diffusely throughout. This sub-epithelial zone contains numerous capillary blood vessels. The central portion of the tissue is composed of denser connective tissue, which is fairly vascular. There are several ducts shown in cross section in the deeper tissue. They are lined by transitional epithelium also. A few of these ducts contain corpora amylacea.

Diagnosis: Small glandular polypus showing a subacute inflammatory reaction.

Case II. S. G. Male. Age forty-eight. Occupation: Tailor. Out-patient department no. 57539. Complaint: Frequency of urination day and night.

Family history: Negative. Past history: Irrelevant. Genito-urinary: Neisser three times, twenty, twelve, and seven years ago. No complications. Lues denied. Frequency of urination started one month ago. Diuria twelve and nycturia twelve. Sexual powers diminished. Physical examination reveals a chronic infection of the prostate and seminal vesicles. There is a left varicocele. Urine culture shows staphylococcus aureus. Guinea-pig inoculation negative for tuberculosis. Blood Wassermann negative. Cysto-urethroscopy: Bladder negative. On right anterior octant of vesical neck is a large sessile polypus. On the left posterior octant is a small sessile polypus. These were removed with the rongeur forceps, and the bases fulgurated. The patient was given one month's rest, after which cysto-urethroscopy revealed no polypi. Massage showed 50 per cent pus. Pus disappeared in two weeks of ordinary routine treatments and has remained clear.

Pathological report (figs. 3 and 4): The surface of the small polypus is covered by transitional epithelium. A great many of the cells are hydropic. In areas along the surface, the epithelium has desquamated, leaving exposed an edematous connective tissue. The epithelium dips down into the sub-epithelial tissue with formation of glandular structures. These are lined by several layers of epithelial cells, which are cuboidal and columnar in type; the superficial layer consisting of mucous cells. Some of these glandular structures which are shown in cross section are rather large and irregular in shape. The stroma of the tissue consists of an edematous reticular connective tissue. There is moderate diffuse infiltration of lymphocytes with an occasional



FIG. 3. SMALL GLANDULAR POLYPUS SHOWING SUBACUTE INFLAMMATORY
REACTION. CASE II
Leitz oc. I, obj. 2

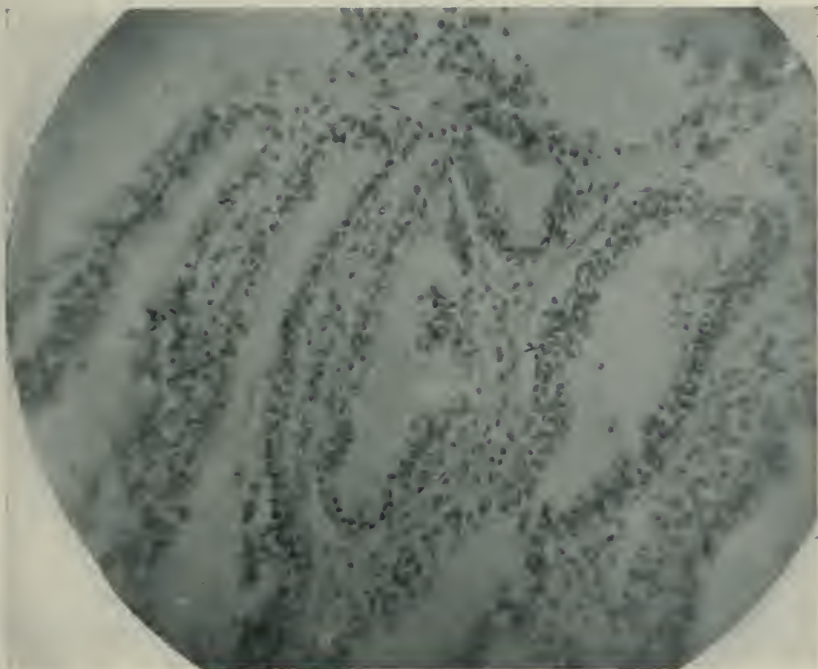


FIG. 4. SMALL GLANDULAR POLYPUS SHOWING SUBACUTE INFLAMMATORY
REACTION. CASE II
Leitz oc. I, obj. 6



FIG. 5. GLANDULAR POLYPUS SHOWING SUBACUTE INFLAMMATORY REACTION.
CASE III

Leitz oc. I, obj. 3

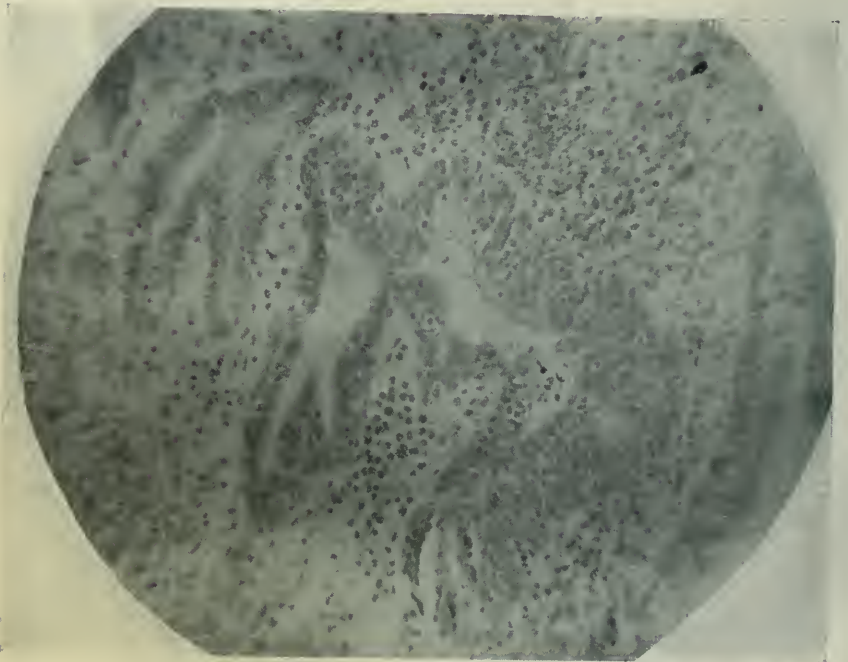


FIG. 6. GLANDULAR POLYPUS SHOWING SUBACUTE INFLAMMATORY REACTION.
CASE III

Leitz oc. I, obj. 6

polymorphonuclear leucocyte and plasma cell. There are also two focal collections of lymphocytes shown in the section. There are several small hemorrhagic areas throughout the stroma and along the denuded surface. This appears to be recent and is probably traumatic.

Diagnosis: Small glandular polypus showing subacute inflammatory reaction.

Case III. A. B. Male. Age thirty-three. Occupation: Seaman. Out-patient no. 25089. Complaint: Morning drop.

Past history: The patient had gonorrhea six years ago and eighteen months ago, which cleared up in about six weeks under the usual routine treatment. No complications. Examination of the lower uro-genital tract: A smear of the morning drop shows no organisms; secretion from prostate shows about 30 per cent pus; the left epididymis is indurated. Ordinary treatment was instituted covering a period of three months. Pus negative. One month's rest—pus reappeared. Cysto-urethroscopy—polypus on infra montane region and verumontanum. Rongeur specimens were obtained and the bases were fulgurated. In two weeks remaining polypus were removed and fulgurated. Cysto-urethroscopy one month later showed no polypi and the infection in the prostate and seminal vesicles had cleared up.

Pathological report (figs. 5 and 6): The tissue consists of a stroma of edematous reticular connective tissue. There is marked diffuse infiltration of lymphocytes with a few polymorphonuclear leucocytes and plasma cells. There is one large hemorrhagic area which shows a marked focal accumulation of lymphocytes with a few plasma and endothelial cells. Around the periphery of the area there are numerous capillary blood vessels. At one end of the section there are numerous glands. These glands are lined by several layers of epithelial cells which are columnar and cuboidal in type. The superficial layer is composed of a mucous type of cell. The surface of the tissue is lined by transitional epithelium. Over a large part of the surface the epithelium has desquamated completely and in other areas the superficial cells have desquamated.

Diagnosis: Glandular polypus showing subacute, inflammatory reaction.

Case IV. J. S. Male. Age twenty-three. Occupation: Riveter. Neisser three years previously. Denies lues. Neisser at present. Urine: Second glass showed *B. coli*, erythrocytes, and pus cells. No tubercle bacilli were found. The patient developed epididymitis.

An epididymotomy was performed in another hospital. One month later patient returned complaining of frequency, especially during the day, sudden interruption of stream and hematuria. No discharge at the meatus. No gonococci found. X-ray of genito-urinary tract showed vesical calculus. This was removed by the suprapubic route. Two months later cysto-urethroscopy showed a large polypus on the verumontanum and two small polypi on the vesical neck. These were removed and the bases fulgurated. He still has prostatitis and seminal vesiculitis which is clearing rapidly.

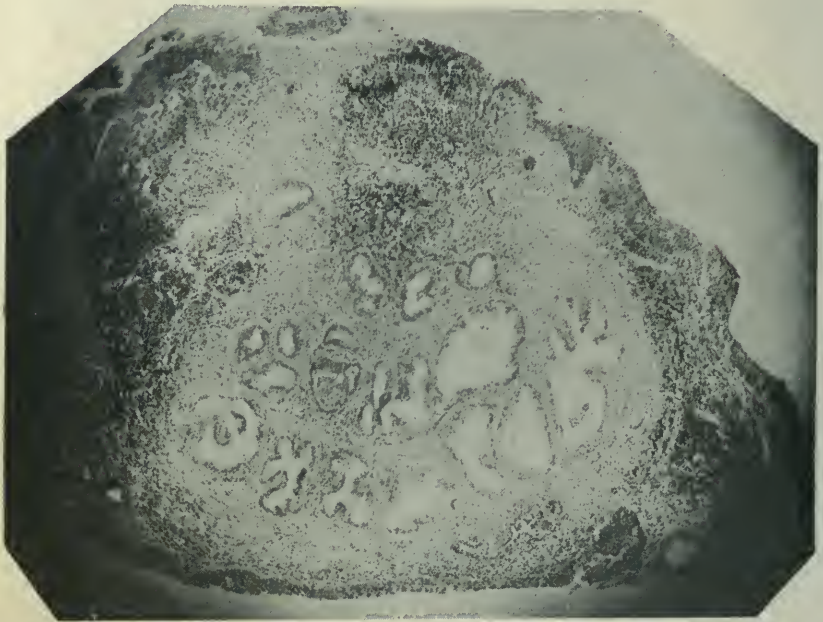


FIG. 7. GLANDULAR POLYPUS SHOWING INFLAMMATORY REACTION. CASE IV
Leitz oc. I, obj. 3

Pathological report: The specimen consists of three small pedunculated tumors, the largest one being about 3 by 2 cm., each of the others being 2 by 1 cm.

The sections of the largest specimen are transverse to the long diameter. The entire surface is covered by transitional epithelium, which is thickened in places. There is one papillary projection from the surface; this has a central stroma of connective tissue, the overlying

epithelium is not thickened. There are several glandular invaginations which are lined by transitional epithelium. In the central portion of the section there are several irregular, glandular structures lined by cuboidal epithelium, which is hyperplastic in places, giving a pseudostratified appearance. Two of these spaces contain granular albumi-

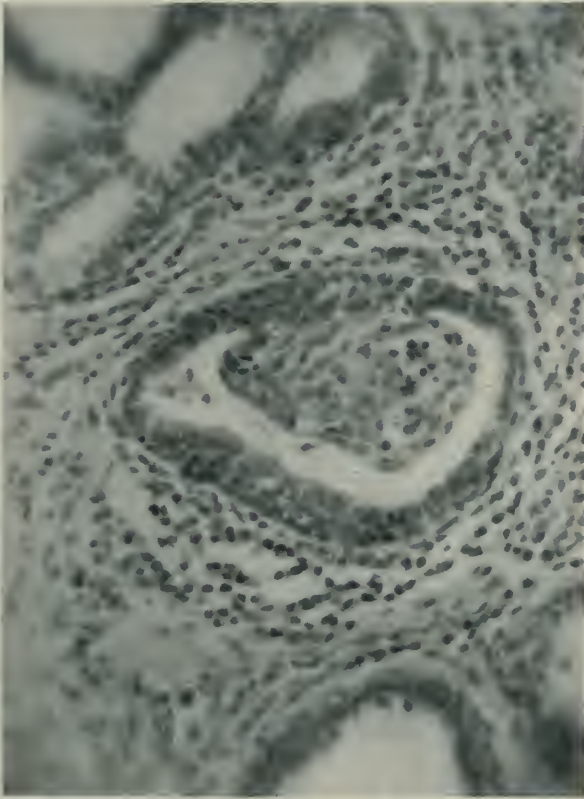


FIG. 8. GLANDULAR POLYPUS SHOWING INFLAMMATORY REACTION. CASE IV
Leitz oc. I, obj. 3

noid material. The stroma consists of rather mature connective tissue which shows diffuse infiltration with lymphocytes. There are several compact focal accumulations of lymphocytes just beneath the surface epithelium. The stroma is fairly vascular. There are two areas of necrosis due to trauma in removal, also areas of traumatic hemorrhage.

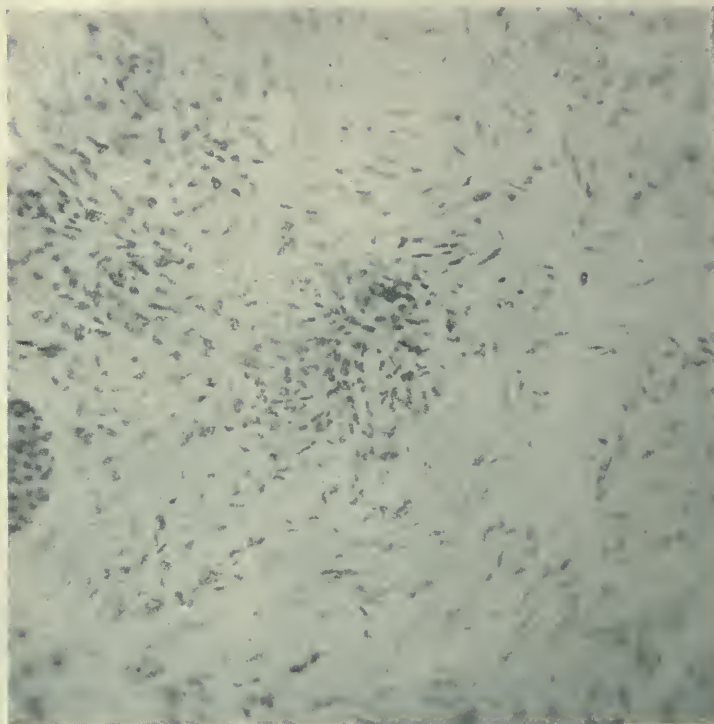


FIG. 9. FIBROUS TYPE OF BENIGN POLYPOID MASS SHOWING CHRONIC INFLAMMATORY REACTION. CASE IV
Leitz oc. I, obj. 3

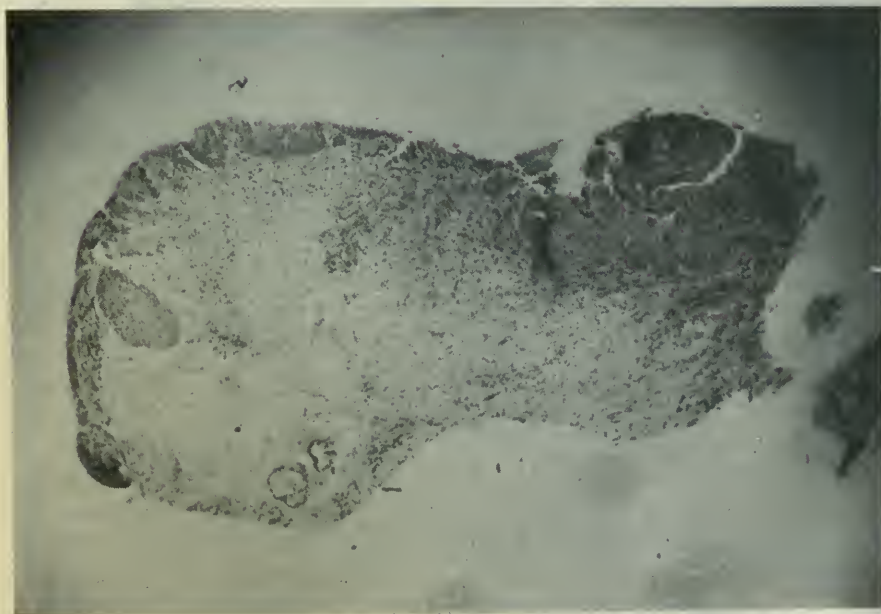


FIG. 10. FIBROUS TYPE OF BENIGN POLYPOID MASS SHOWING CHRONIC INFLAMMATORY REACTION. CASE IV
Leitz oc. I, obj. 6

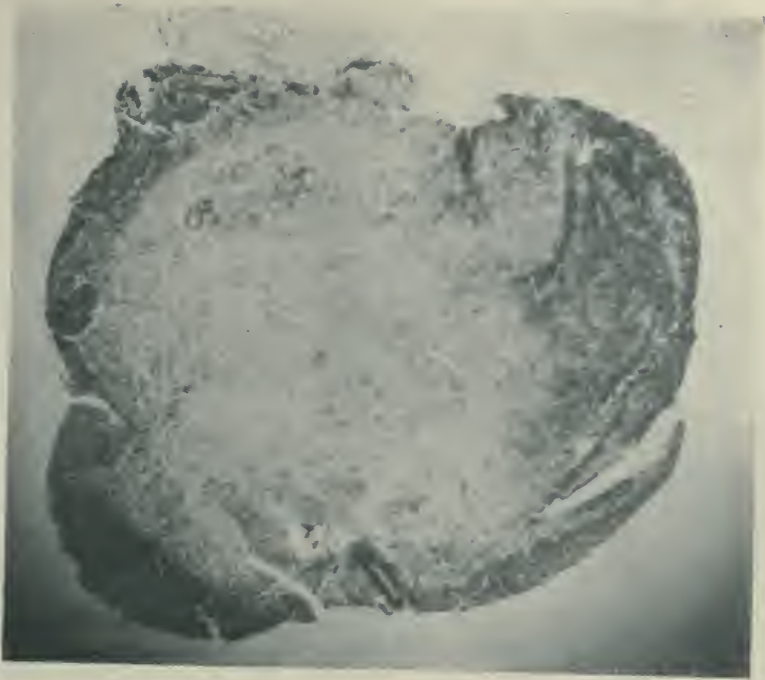


FIG. 11. FIBROUS TYPE OF POLYPOID MASS SHOWING CHRONIC INFLAMMATORY
REACTION. CASE IV
Leitz oc. I, obj. 3

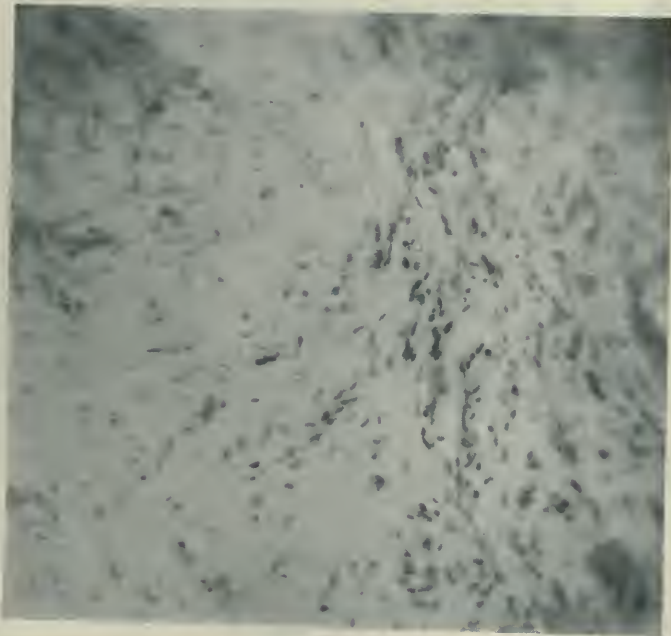


FIG. 12. FIBROUS TYPE OF POLYPOID MASS SHOWING CHRONIC INFLAMMATORY
REACTION. CASE IV
Leitz oc. I, obj. 6

The two smaller specimens were sectioned parallel to their long axis. These are similar to the larger specimen in every respect, except that the glandular structures are less numerous.

Diagnosis: Adenomatous polypi showing subacute inflammatory reaction.

Case V. I. B. Male. Age forty. Occupation: Ranch hand. Out-patient department no. 54733.

The family history is negative. He denies Neisser. He comes to the clinic complaining of occasional nycturia. There is a peculiar pain in the perineum. He has a morning drop. There is more or less continual dull lumbo-sacral pain which is uninfluenced by rest or exercise. The sexual power, however, is good. The urine is negative, culture negative, and inoculation of guinea-pigs for tuberculosis is negative. The blood Wassermann is negative. The lungs are normal. The lower urogenital tract shows chronic prostatitis. Cysto-urethroscopic examination revealed three fairly large, pink, sessile masses on the right and left anterior octants of the vesical neck. These show areas of hyperemia, and blood vessels are seen to course over their surfaces. The adjacent mucosa is congested. The bladder and prostatic urethra are otherwise of no interest.

These masses were removed with the ronguer forceps and show the following histological structure.

Pathological report: The small piece of tissue is composed of edematous reticular connective tissue. There is diffuse infiltration of plasma cells with a few polymorphonuclear leucocytes. There are areas in the stroma in which the tissue is disorganized, and there is a diffusion of chromatin material. This is most probably due to crushing of the tissue in the process of removal. There are two small glands in the section and these are lined by several layers of cuboidal and columnar epithelium. There are a few dilated capillary blood vessels throughout the stroma. The surface is irregular, due to crypt-like depressions. Over a part of the surface the epithelium has desquamated leaving only the basal layers of cells.

Diagnosis: Small polypoid mass showing subacute inflammatory reaction.

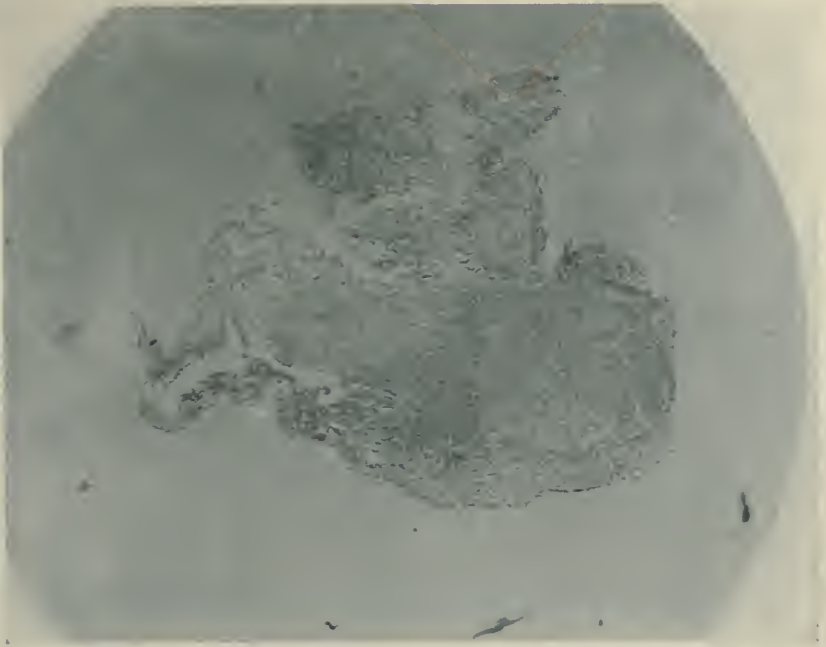


FIG. 13. SMALL POLYPOID MASS SHOWING SUBACUTE INFLAMMATORY REACTION.
CASE V
Leitz oc. I, obj. 3

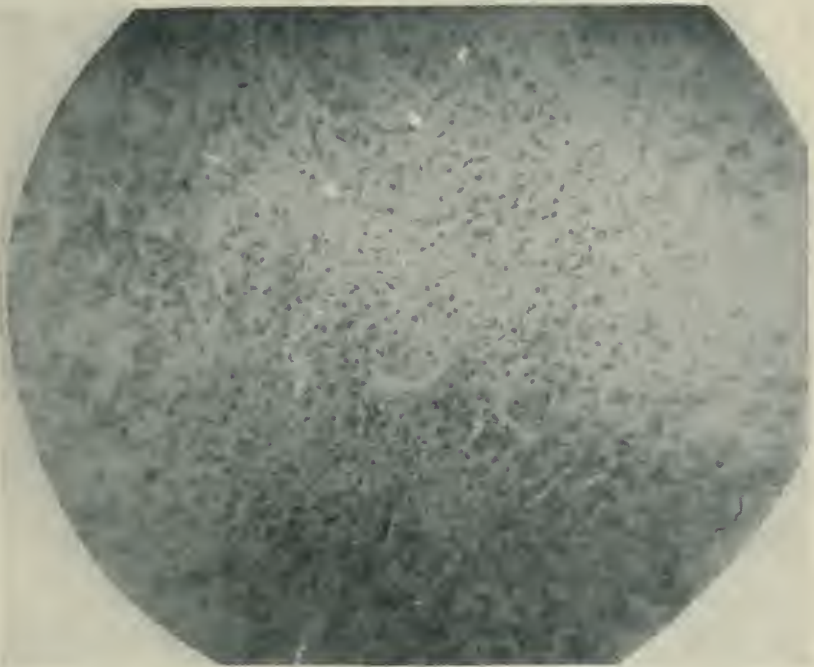


FIG. 14. SMALL POLYPOID MASS SHOWING SUBACUTE INFLAMMATORY REACTION.
CASE V
Leitz oc. I, obj. 6

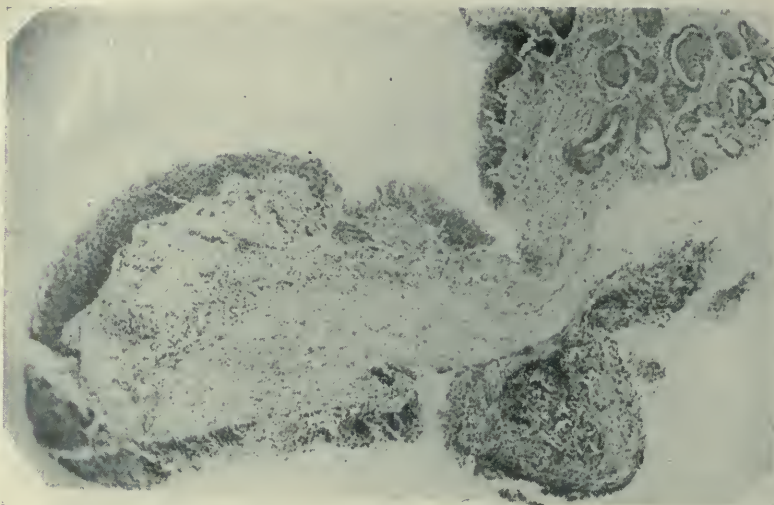


FIG. 15. POLYPOID EXCRESCENCE SHOWING SUBACUTE INFLAMMATORY REACTION.
 CASE VI
 Leitz oc. I, obj. 3

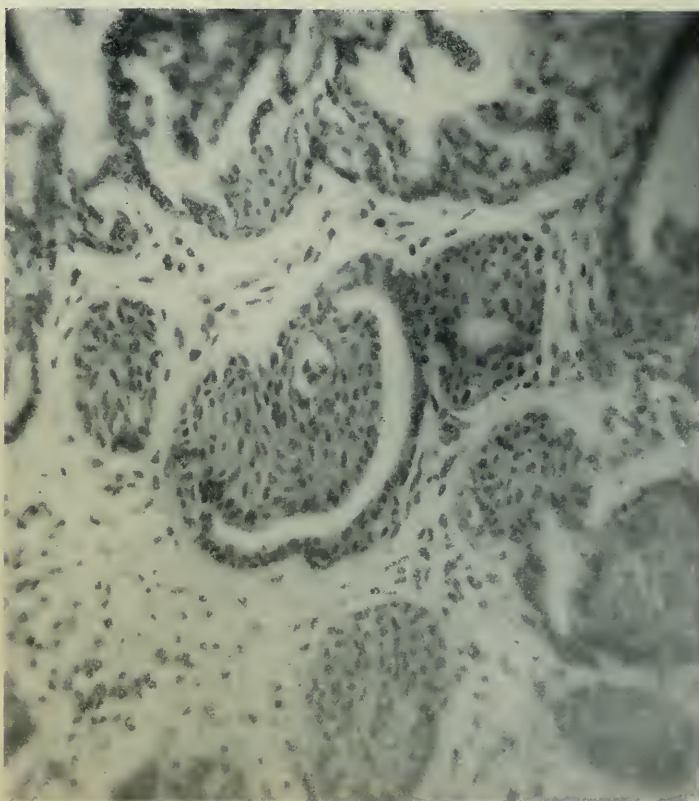


FIG. 16. POLYPOID EXCRESCENCE SHOWING SUBACUTE INFLAMMATORY REACTION.
 CASE VI
 Leitz oc. I, obj. 6

Case VI. J. M. Male. Age sixty-three. Occupation: Fireman. Out-patient department no. 55283. Entered August 4, 1919.

Family history negative. Past history: Cataract operation and fracture of the left fibula. Operation for vesical calculus six years ago. Genito-urinary: He had gonorrhea four times and treated himself. Chancre thirty-five years ago for which he received no treatment. Present illness: Difficulty in urination, diuria, and nycturia main urinary symptoms. He is a diabetic. Rectal examination: Bilateral hypertrophy of prostate. He was sent to the medical clinic for treatment of diabetes. After the urine was found to be sugar free a prostatectomy was performed. Three months later, he showed numerous small nodules in the posterior urethra. Specimens removed by rongeur and the bases fulgurated.

Pathological report: Microscopic examination shows a slight irregular thickening of the epithelium beneath which there is irregular edema, dilatation of the vessels, and irregular infiltration with lymphocytes and plasma cells. The ducts from a number of glands in the section show considerable thickening and transitional type of epithelium.

Diagnosis: Polypoid exerescence showing subacute inflammatory reaction.

Case VII. M. Q. Male. Age thirty-five. Occupation: Laborer. Out-patient department no. 64017. Entered June 23, 1919. Complaint: Gonorrhea.

Family history: Irrelevant. Past history: Unimportant. Genito-urinary: Gonorrhea in 1917, treated by druggist, of three months duration. Left epididymitis. Gonorrhea one month ago. Treated by druggist. At present, no organisms. He shows prostatitis and seminal vesiculitis. Pus 15 per cent. Cysto-urethroscopy: Large polypus on the anterior aspect of the vesical neck was removed with rongeur forceps and the bases fulgurated. Results: February 2, 6, and 9, 1920, secretions negative.

Pathological report: Microscopically, this specimen consists of a stroma of edematous connective tissue, throughout which are numerous small capillary blood vessels. The surface is lined by transitional epithelium. The cells of the epithelium are hydropic in appearance. There is a diffuse infiltration of lymphocytes and plasma cells throughout the subepithelial connective tissue. A few lymphocytes have also invaded the surface epithelium. There are no glands present in the sections.

Diagnosis: Fibrous type of polypoid mass showing chronic inflammatory reaction.



FIG. 17. FIBROUS TYPE OF POLYPOID MASS SHOWING CHRONIC INFLAMMATORY
REACTION. CASE VII
Leitz oc. I, obj. 3

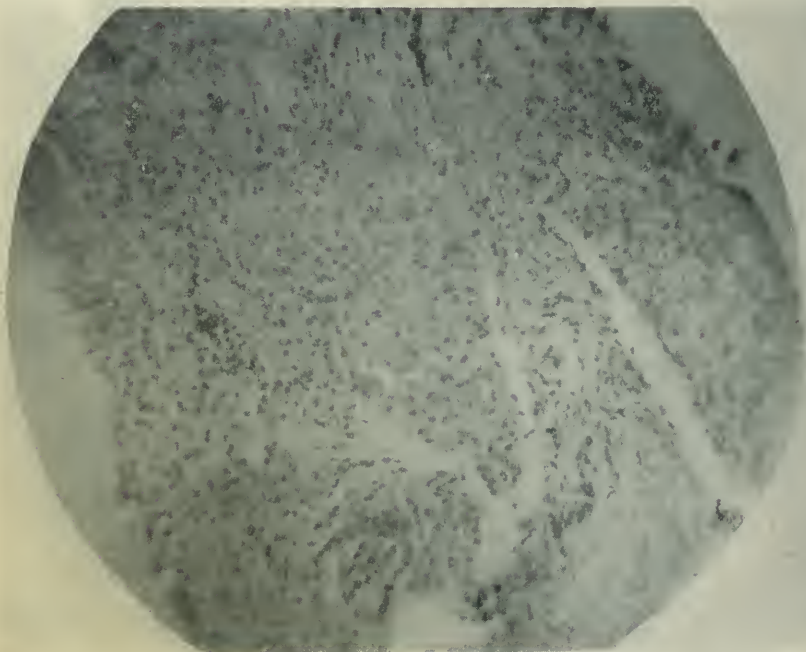


FIG. 18. FIBROUS TYPE OF POLYPOID MASS SHOWING CHRONIC INFLAMMATORY
REACTION. CASE VII
Leitz oc. I, obj. 6

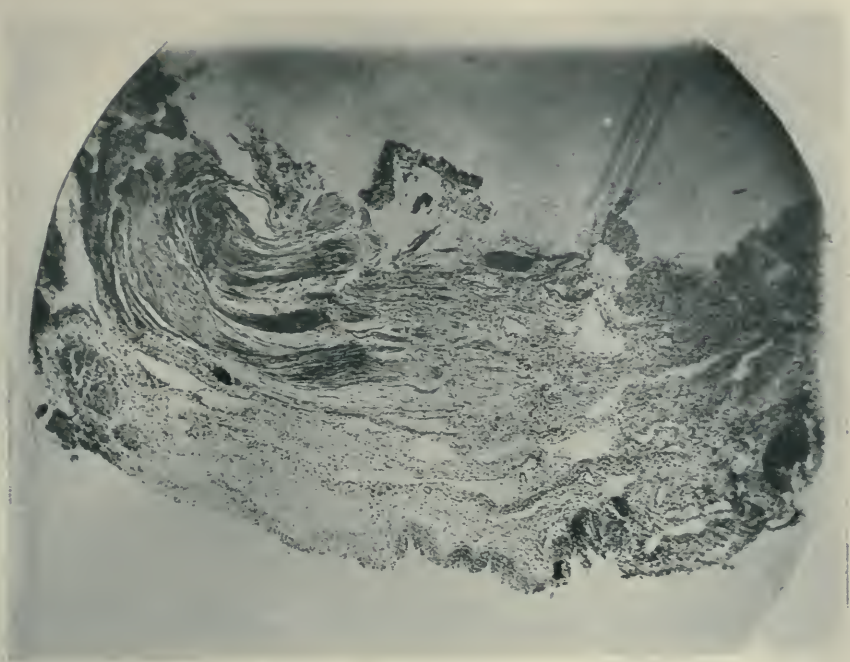


FIG. 19. SMALL INFLAMMATORY EXCRESCENCE OF THE MUCOSA OF THE VESICAL
NECK. CASE VIII
Leitz oc. I, obj. 3

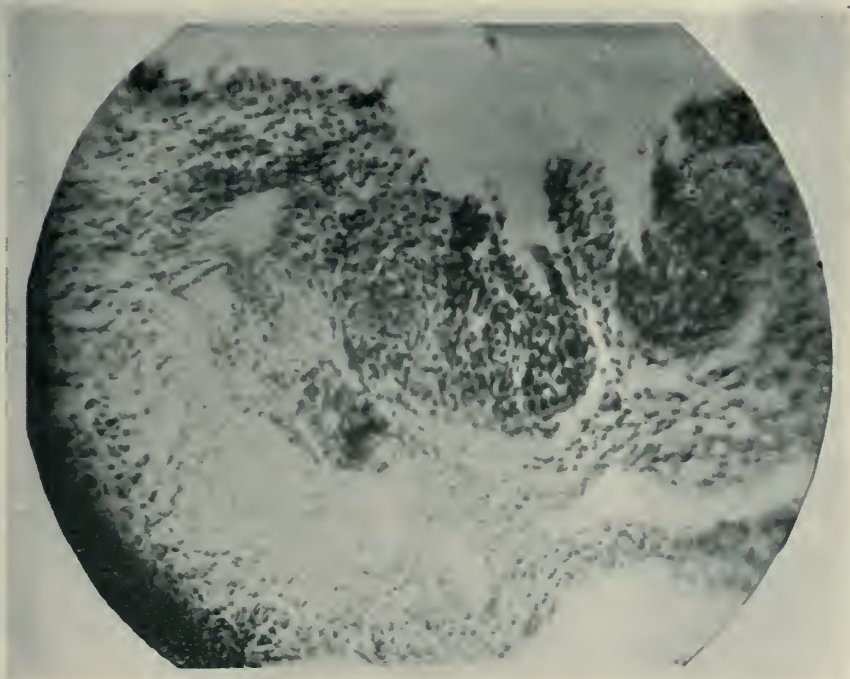


FIG. 20. SMALL INFLAMMATORY EXCRESCENCE OF THE MUCOSA OF THE VESICAL
NECK. CASE VIII
Leitz oc. I, obj. 6

Case VIII. L. F. Male. Age thirty-five. Occupation: Porter. Out-patient department no. 52867.

The family history is irrelevant. He had six attacks of gonorrhea of an average duration of six to eight weeks for which he received no treatment, the last attack occurring two months ago. He had a chancre ten years previously followed by no secondaries. This was not treated. He now complains of occasional nycturia and increased frequency. There is no morning drop. He has dull lumbosacral pain uninfluenced by rest or exercise. The sexual powers are diminished. The urines were clear but contained shreds in the first and third glasses and were negative to culture and to guinea-pig inoculation for tuberculosis. The blood Wassermann was triple positive. The lower urogenital tract showed prostatitis and seminal vesiculitis. Cystourethroscopic examination reveals some relaxation of the vesical neck. On the anterior right and left octant of the vesical neck are two sessile, pale pink, excrescences over which blood vessels are seen to course. The adjacent mucosa is congested. The bladder walls show moderate coarse trabeculations. Excrescences removed in usual way and the bases fulgurated.

Pathological report: The specimen consists of an elongated irregular mass of tissue which is covered on three sides by transitional epithelium. The epithelial layer is thickened in places and these areas show a desquamation of the superficial cells. At one pole of the section the epithelial surface is thrown into papillary folds and the epithelial layer appears thickened. At two points there are invaginations of the epithelium into the deeper tissues. These are shown in cross section. Beneath the epithelium there is a zone of loose reticular tissue. The tissue contains numerous capillary blood vessels. There is a diffuse distribution of lymphocytes throughout this zone. There are also a few eosinophiles, and numerous, rather large, fibroblasts. At the base of the section there is included a small section of smooth muscle.

Diagnosis: Small inflammatory excrescence of the mucosa of the bladder.

TREATMENT

Growths of the urethra have long been recognized and various instruments devised for their removal. About 1607, Layseau removed a papillary vegetation from the urethra of Henri IV which had caused urinary obstruction. Bell (31), in 1820,

removed a warty substance formed within the anterior urethra with a scissors and a ligature. Grunfeld (32), in 1881, removed urethral polypi by means of a snare and scissors through an endoscope. Oberländer (33), six years later, introduced his tampon erasement method. This consisted of grasping the polypus with two tampons passed through an endoscope and with a twisting motion the polypi were torn loose from their bases. The good results claimed by this surgeon were not substantiated by Klotz (4) and other investigators, and the method soon fell into disrepute. Another ingenious device for removing urethral tumors was the guillotine. In 1886 Klotz (4) reported one hundred tumors removed from various parts of the urethra with a strong forceps and a curette. Cauterizing agents of all descriptions have been employed since the introduction of the endoscope by Désormeaux (9). Oftentimes they serve only to partially destroy the tumor even after numerous applications. Randall (22) states that nitrate of silver is absolutely inadequate and that they should be removed with a snare and alligator forceps and the bases cauterized. With the advent of the cystourethroscope of Greenberg (34), Goldschmidt, Bransford Lewis, Buerger (35) and McCarthy, which is used with water dilatation, the diagnosis and treatment of these tumors have been greatly enhanced. Through this instrument all the mechanical devices for removal of bladder and urethral neoplasms can be used with ease. Later contributors to the literature, among them Lewis, Greenberg (34), Lewin (36), Buerger (37), Wolbarst (12), Watson (38), Martin (39), and others, have used the high frequency electric current to permanently destroy these tumors and they report excellent results.

We applied the following methods of treatment:

1. Dilatation of the urethra by the use of sounds or the Kollmann dilator. This is the best form of treatment for the simple edematous excrescences of the vesical neck and the urethral wall. This type of urethral tumors usually clears up with this form of treatment and rarely requires fulguration.

2. Direct application of cauterizing agents such as nitrate of silver, the stronger acids, etc.

3. Snaring through the endoscope and the cystoscope.
4. Excision by means of scissors.
5. Crushing the pedicle by means of rongeur forceps and the removal of the polypus.
6. Destruction by use of the actual cautery.
7. Electro-cautery.

The most satisfactory of these methods is the use of the electro-cautery. The small Wappler electrode is best adapted to this purpose, because it can be easily applied to the pathological point only. The D'Arsonval current, although the most destructive to living cells, we found to give the best results. By use of the snare, and the rongeur forceps, these tumors are easily removed, but the base is more or less intact and may be the site of recurrence and hemorrhage.

RESULTS

After the destruction of these polypi the patient is given one month's rest. The treatment of the remaining pathological condition in the prostate and seminal vesicles is then continued. The following results were obtained: Fifty cases or 73.7 per cent showed marked improvement with probable cure. Fourteen cases or 20.5 per cent showed slight improvement. Four cases or 5.8 per cent showed no improvement.

At intervals of six months to two years after removal of the tumors fifty of the sixty-eight cases were observed with the cysto-urethroscope. Two only showed recurrence of the polypi within this interval.

A number of the most typical tumors in the three groups described above were removed with the rongeur forceps and studied histologically. These are described with the individual case reports.

DISCUSSION AND SUMMARY

The unsatisfactory response to treatment of many cases of chronic infection of the lower urogenital tract in males justifies a search into the cause for the continued presence of disease.

Many such patients were below par presenting lesions in the gastro-intestinal tract, syphilis, tuberculosis or other general infections which lowered their resistance, making the cure of the prostatitis almost impossible. However in another group of cases, where there occurred a persistent reappearance of pus or a continuance of symptoms in spite of long continued treatment of the usual routine type, careful investigation with the cysto-urethroscope, revealed tumors in the prostatic urethra and bladder neck. These, through irritation, caused a continuance of the pathological condition in the prostate.

In twenty-seven hundred cysto-urethroscopic observations, sixty-eight tumors were found. The symptoms complained of were those of chronic prostatitis with the following symptoms predominating (also see table 1):

	<i>per cent</i>
Peculiar pain or discomfort in the perineum	84.0
Pain or itching at or inside the meatus	75.0
Diminished sexual power	14.0
Premature and painful ejaculation	11.0
Sensation of mass or foreign body in the urethra	4.0
Ball-valve interference of the urinary stream	1.5

The normal structure of the urethra and the bladder neck with its indentations of the transitional epithelium forming more or less developed mucous glands offers an easy avenue for infection. As the inflammation proceeds, these glands increase in size, the ducts are often occluded, project and encroach upon the lumen of the prostatic urethra, often commencing as a small excrescence of the urethral wall or the bladder neck and later developing into a tumor giving the appearance of a sessile polypoid mass or polypus. The classification of these tumors morphologically is as follows: (1) The true polypus with a pedunculated base, (2) the polypoid mass with a sessile base, (3) a simple edematous excrescence. Either the true polypus or polypoid mass may be villous. The pathological nature of these tumors can be ascertained by histological study and should be carried out in all cases to arrive at a proper diagnosis. This may be done in the course of treatment by removing the mass

with the rongeur forceps and fulgurating the base. Two general types were observed: (1) Glandular type in which the glandular tissue is predominant; (2) the fibrous type in which the fibrous connective tissue is predominant. Both show a thickening of the transitional epithelium at certain points which is invaded by polymorphonuclear leucocytes, a sub-epithelial zone of loose edematous reticular connective tissue which is infiltrated with lymphocytes, polymorphonuclear leucocytes and plasma cells, and contains numerous capillary blood vessels. The central portion of these tumors shows numerous blood vessels, is composed of either a denser, more developed connective tissue or of glandular tissue, the glands being lined by several layers of cuboidal and columnar cells, the superficial layer being mucoid in type. In short, all these tumors that were studied show inflammatory changes due to continued infection. The glandular type is not a true growth in the true sense of the word but rather a proliferation of the many shaped normal mucous glands, stimulated by infection. Corpora amylacea were found only in tumors arising from the verumontanum. It is evident, in cases of chronic prostatitis and seminal vesiculitis that these tumors with their existing infection act as a source of irritation and cause reinfection of the seminal vesicles and prostate. On the other hand, they can cause a continuence of the general symptoms of prostatitis and seminal vesiculitis, after these organs have apparently been cleared up, no pus being found in the secretions on repeated massage. In such cases, after removal of these tumors, 73.7 per cent showed marked improvement with probable cure, 20.5 per cent showed slight improvement, 5.8 per cent showed no improvement.

It is interesting to note that of the four cases showing no improvement, two had a definite history of syphilitic infection with a triple positive blood Wassermann. This was being treated concurrently. The remaining two discontinued treatment and could not be followed a sufficient time to justify an accurate statement in regard to their condition.

CONCLUSIONS

1. In the treatment of resistant forms of chronic prostatitis, a complete cysto-urethroscopic examination is indicated in order to rule out the presence of foci of infection such as polypi, polypoid masses and edematous excrescences on the bladder neck or urethral wall.

2. Observation through the cysto-urethroscope revealed three types of tumors, the morphological appearances of which were as follows:

a. True polypi with pedunculated bases, *b.* Polypoid masses with sessile bases, *c.* Simple edematous excrescence.

3. Histological study of these tumors shows them to be made up either of glandular or of connective tissue with a general infiltration of round cells, polymorphonuclear leucocytes and plasma cells throughout the growth, associated with chronic granulation tissue due to a focus of infection which is continued.

4. In those cases in which the vesicular and prostatic secretions were found to be greatly improved, where, however, a continuance of symptoms occurred and polypi or polypoid masses existed, the symptoms did not clear up until these tumors were finally destroyed by fulguration.

5. It is pointed out that these growths can act as a source of irritation and so cause a reinfection of the prostate and the seminal vesicles. Upon the removal of these tumors 73 per cent of these resistant cases showed marked improvement with probable cure, 20.5 per cent showed slight improvement, and 5.8 per cent showed no improvement.

We wish to express our thanks to Dr. G. Y. Rusk for assistance in the pathological study of these tumors and to Dr. A. W. Lee for the preparation of photomicrographs.

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PLATE 1

Upper left: Three edematous excrescences on the right anterior aspect of the vesical neck.

Lower left: Polypoid mass on left lateral aspect of the bladder neck.

Center: Three small polypi.

Right: A rather long polypus in the posterior urethra, projecting into the bladder, with a smaller polypus beside it.



PLATE 2

Right: Two polypoid masses on the anterior aspect of the vesical neck and a villous excrescence which later proved to be carcinoma.

Left: From the same patient, two tumors from the bladder. These are apparently polypi of the villous type but were demonstrated after pathological section to be carcinoma.

PLATE 3

True polypus with a pedunculated base and a polypoid mass with a sessile base situated together on the vesical neck.



THE FOLLOW-UP RECORD IN CASES OF TUMOR OF THE BLADDER

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The tendency of tumors of the bladder of all grades of malignancy to recur, in spite of the method of removal or the thoroughness of the operation, has long been recognized. It has been the custom in the Mayo Clinic for many years to advise patients who have had such tumors removed to return at stated times for cystoscopic examination. The intervals between should be: three months, three months, six months, one year, and one year; covering a total of three years' time. If there is no recurrence during this period it may be considered reasonably certain that there will be no further trouble. A recurrence of the growth, however, necessitates a recurrence of the treatment and of examinations.

Many of our patients have returned for cystoscopy at the times advised, and in this way a number of small recurrences were discovered early and destroyed by fulguration or radium. There were, however, a large percentage of patients who did not return as long as they had no symptoms, but who returned months and even years later than advised, with recurrences of such extent that fulguration was impossible. In some cases even a secondary resection could not be performed, or if performed gave little chance of permanent relief.

Several months ago in an effort to induce a larger percentage of patients to return at the time designated we started an individual follow-up system by means of a card as follows:

two weeks after the second, insisting as forcibly as possible, on the patient's return. These letters are checked on the card as sent. The date of the patient's return, the presence of recurrence, the treatment, the prognosis, and the date of the next return are noted at each dismissal. Discontinuance of the follow-up of any person is indicated by stating the reason, thus, "Cured," "Recurrence, too extensive," "Dead," "Would not return," "Referred to Dr. Smith." When completed, the card is filed in the rear of the current cards under an index showing the results. The heading "Remarks" will take care of notes of special interest regarding the individual case.

URINARY ANTISEPSIS—THE SECRETION OF ANTISEPTIC URINE BY MAN FOLLOWING THE ORAL ADMINISTRATION OF PROFLAVINE AND ACRIFLAVINE—PRELIMINARY REPORT¹

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The problem of internal urinary antiseptics, involving the principles of specific chemotherapy, offers a particularly interesting field for investigation. Owing to the proved ability of the kidney to select from the blood stream and concentrate in the urine compounds of certain chemical structure, the opportunity is afforded of localizing the antiseptic agent in that portion of the body where antiseptic action is desired—the urinary tract.

This problem is of very great practical as well as theoretical interest. To those who have had to deal with chronic inflammatory conditions of the urinary tract, the lack and the need of an efficient drug for this purpose is only too apparent. A survey of the medical literature pertaining to urinary antiseptics reveals a surprising absence of sound experimental or clinical evidence of the fitness of any drug for this purpose. Urotropin affords a partial exception to this statement. It is an established fact that urotropin in adequate dosage, through the

¹These investigations were begun in the laboratories of the Brady Urological Institute, the Johns Hopkins Hospital and continued in the laboratories of the University of Nebraska College of Medicine, with the aid of an appropriation by the United States Interdepartmental Social Hygiene Board.

It is to be particularly noted that the results tabulated below apply *only* to French and English preparations of proflavine and acriflavine, the commercial importation of which is prohibited by the Chemical Foundation. Since the synthesis and purification of proflavine and acriflavine is a difficult and complicated process, and since there has been recognized a variation in the clinical efficiency of these dyes, the author assumes no responsibility for failure to duplicate the above results; or for toxic effects produced by the use of other preparations, which may and may not be less pure, less efficient and more toxic.

liberation of formalin in an *acid* urine, exerts a definite antiseptic action. But this drug has its distinct and well known limitations. The liberation of formalin at the kidney level is open to question. In alkaline urine, the drug is inert. Hematuria following the administration of urotropin in ordinary dosage is not rare. The most serious argument against urotropin, however, is its very frequent clinical inefficiency. While it is not uncommon for text-books to briefly dismiss the subject of urinary infection with the vague recommendation of "some urinary antiseptic," authoritative writers agree that in the treatment of infections of the urinary tract our two most important measures are drainage and diuresis. These same authors frankly admit that by way of medicinal treatment we are limited to a choice of either urotropin or alkalinization, neither of which is dependable. Keyes (1), considering urinary antiseptics, discards all but urotropin, and the chief value of this he limits to prophylaxis following instrumentation. It is not the purpose of this paper to discuss further the evident lack of a drug suitable for this use.

The compound ideally adapted for the purpose of internal urinary antisepsis should be chemically stable, and relatively non-toxic and non-irritating; should be antiseptic in high dilution in urine of any reaction; and should be eliminated unchanged in high percentage by the kidney. Clinically, there is no such drug known.

Previous publications (Davis (2), Davis and White (3)) have pointed out the possibilities in this field offered by synthetic chemistry, and have demonstrated a certain relationship between chemical structure and renal excretion. Further studies (Davis, White and Rosen (4)) have shown that chlor-mercury-fluorescein, an organic, mercury-containing, phthalein derivative, is experimentally successful in causing the secretion of antiseptic urine following the intravenous administration to rabbits and dogs, in amounts far below toxic dosage. Clinical use of this drug was not attempted on account of its mercury content. Further investigation of the same class of compounds resulted in the synthesis of mercurochrome-220 (Young, Swartz and

White (5)), which has been shown to be of value, not for internal medication but used in the form of urethral or bladder instillations. It has also been shown that the intravenous administration of proflavine (diamino acridinium sulphate) and acriflavine (diamino methyl acridinium chloride) to rabbits will cause the secretion of antiseptic urine (Davis and White (6)). Although this latter fact was published in 1918, investigation of these two drugs was temporarily discontinued on account of the war, and because preliminary experiments indicated that oral administration was unsuccessful. A recent study of more than two hundred anilin dyes (Davis (7)), as to their fitness for the purpose of urinary antiseptics, indicated certain dye groups (azine, xanthone, triphenylmethane, and acridine) which gave particular promise of value, and showed that of the entire group proflavine and acriflavine were the only two experimentally possessing all the required properties. Inasmuch as the above study was preceded by an investigation of 200 other compounds (2), it is to be noted that the following experiments, involving the administration of proflavine and acriflavine to man, were undertaken only after a process of elimination of more than 400 compounds.

ANTISEPTIC VALUE OF ACRIFLAVINE IN URINE IN VITRO

As detailed in previous publications, preliminary experiments were undertaken to determine the antiseptic value of proflavine and acriflavine in vitro, using urine as a culture medium. Since the importance of the hydrogen ion concentration of the urine, as a factor in influencing the potency of a given antiseptic, has been demonstrated, it was necessary to use from day to day samples of urine titrated to definite reactions. Table 1 shows the efficiency of acriflavine in both acid (pH 6.0) and alkaline (pH 8.0) urine. According to previously described technique, varying dilutions of the drug, in acid and alkaline urines, were inoculated with *B. coli* and *S. aureus*. The inoculated dilutions were incubated for twenty-four hours, and samples (0.1 cc.) were then removed from the tubes and plated, to determine

whether growth or death had taken place during the incubation period. Attention is called to the remarkable effect which slight variation in the hydrogen ion concentration of a urine medium may have in influencing the efficiency of an antiseptic. Acriflavine restrains the growth of both organisms in alkaline (pH 8.0) urine in very high dilution (1:100,000). In acid (pH 6.0) urine it is almost equally efficient against the staphylococcus, but loses its effect on the colon bacillus in a dilution between 1:5,000 and 1:7,500. Therefore, in order to obtain results by the internal administration of this dye the importance of rendering the urine alkaline is clearly indicated.

TABLE 1
The antiseptic strength of acriflavine diluted in urine

	COLON BACILLUS		STAPHYLOCOCCUS AUREUS	
	Acid urine (pH 6.0)	Alkaline urine (pH 8.0)	Acid urine (pH 6.0)	Alkaline urine (pH 8.0)
Dilution inhibiting development.....	1:5,000	1:100,000	1: 75,000	1:100,000
Dilution permitting growth..	1:7,500	1:200,000*	1:100,000*	1:200,000*

* In repeating the experiment several times it was observed that even these extreme dilutions usually killed the organism, but occasionally permitted growth. This discrepancy was probably due to variations in the composition of the urine, other factors being constant.

SECRETION OF ANTISEPTIC URINE BY RABBITS

Bearing in mind that a much greater efficiency is to be expected in alkaline urine, in conducting experiments with rabbits it was considered advisable to administer sodium bicarbonate along with the dye. Samples of urine obtained by catheterization from six rabbits were inoculated, incubated for twenty-four hours, then plated, according to previously described technique. As indicated in table 2, by the infinity sign (∞), in each instance the rabbit urine proved to be a suitable culture medium for both colon bacillus and staphylococcus. On the following day the same process was repeated both before and after the administration (by stomach tube) of sodium bicarbonate, 4 grams.

In no instance did the alkalinization alter the suitability of the rabbit urine as a culture medium. On the third day, together with the same dose of sodium bicarbonate, was given proflavine, 0.03 gram per kilo. Before drug administration, in all samples of urine the organisms grew. Four hours later, samples of urine obtained by the same method, and subjected to identically the

TABLE 2

The secretion of antiseptic urine by rabbits following the oral administration of proflavine

RABBIT	COLUMNS BELOW INDICATE NUMBER OF COLONIES WHICH DEVELOPED IN AGAR PLATE CONTAINING 0.1 CC. OF URINE TRANSFERRED FROM TUBE WHICH HAD PREVIOUSLY BEEN INOCULATED AND INCUBATED FOR 24 HOURS					
	May 20	May 21		May 22		
	No drug administration this date	Urine obtained before drug administration	Urine obtained four hours after administration of sodium bicarbonate	Urine obtained before drug administration	Urine obtained four hours after administration of sodium bicarbonate and proflavine	H-ion concentration urine obtained four hours after drug administration
	C S	C S	C S	C S	C S	
103	∞ ∞	∞ ∞	∞ ∞	∞ ∞	∞ ∞	5.8
104	∞ ∞	∞ ∞	∞ ∞	∞ ∞	∞ ∞	8.2
107	∞ ∞	∞ ∞	∞ ∞	∞ ∞	∞ ∞	8.2
59	∞ ∞	∞ ∞	∞ ∞	∞ ∞	∞ ∞	8.0
84	∞ ∞	∞ ∞	∞ ∞	∞ ∞	∞ ∞	8.4
100	∞ ∞	∞ ∞	∞ ∞	∞ ∞	∞ ∞	7.8

C = *Colon bacillus*; S = *Staphylococcus albus*.

Dose of sodium bicarbonate = 4 grams. Dose of proflavine = 0.03 gram per liter.

In this table, and other tables, all inoculations were with one loop of a twenty-four-hour broth culture of the designated organism.

0 = No colonies; ∞ = an infinite number of colonies.

same process, killed the organisms in the case of every rabbit excepting number 103. A glance at the column in table 2 indicating hydrogen ion concentration shows that the urine from rabbit number 103 was the only specimen with an *acid* reaction. Therefore, rabbit urine, obtained four hours after the oral administration of proflavine (0.03 gram per kilo) will kill colon bacilli and staphylococci, provided the reaction is *alkaline*.

TOXICITY

Preliminary experiments in toxicity indicate that while both proflavine and acriflavine may have toxic effects in large dosage, the amount necessary to produce a distinct antiseptic effect in the urine is exceedingly minute in comparison. Rabbits (weighing 2 kilos) were given as much as 0.2 gram at a single dose, with no apparent effect whatever, while as small an amount as 0.05 gram, given to a man (weighing 70 kilos), has been shown to exert a distinct antiseptic action in the urine for a period of several hours.

More important than the effect of a single large dose is the effect of long-continued administration of small amounts. Rabbits were given daily dosage of 0.01 gram per kilo (actual dose 0.02 to 0.03 gram), through a stomach tube, over a period of thirty days. Proflavine was used in one series; acriflavine in another. In each series of three rabbits, one lost weight and finally died in cachexia. Autopsies were negative. Microscopic sections showed no changes in kidney and liver excepting those of inanition. The remainder of these rabbits, under the same living conditions, and subjected to the same dosage, maintained their weight, or gained weight, and remained in perfect health. When sacrificed three months later, autopsies were negative, and sections of kidney and liver were normal, excepting for doubtful cloudy swelling in some of the liver sections.

Young rabbits less than a month old were given daily dosage of 0.005 gram for thirty days, two receiving acriflavine and two proflavine. One of each of these two pair died, as did also one of the two controls from the same litter. The others gained weight and reached maturity, with no apparent effect whatever from the drug.

As to subjective symptoms produced following administration to patients, a certain percentage (about 30 per cent) complained of nausea following larger dosage (0.3 gram). This was almost never the case after 0.1 gram. Not a few noted a mild catharsis; in fact, this information was volunteered by a sufficient number of patients to justify the conclusion that both these drugs exert a definite cathartic action.

In conclusion, it may be said that while the single antiseptis-producing dose (0.01 gram) is exceedingly minute, considering that seventy times this amount (figuring relative weights) has been safely administered to rabbits at a single dose, yet there has not been sufficient experimental work to justify indiscriminate use of large or long-continued dosage.

SECRETION OF ANTISEPTIC URINE BY MAN

The experimental efficiency of these dyes having been proved with rabbits, and safe dosage having been determined by experiments in toxicity, it then remained to conduct similar experiments with man. The dyes were administered to normal individuals, the purpose being not to attempt clinical cures of existing urinary infections, but to demonstrate antiseptic action in specimens of urine voided after dye administration.

The technique was identical with that carried out with rabbits. In each instance a specimen of urine obtained before drug-administration was used as a control, all experiments not so controlled being discarded. Dosage varied from 0.05 to 0.5 gram, as indicated in tables 3 and 4. Specimens of urine were obtained by voiding into a sterile (second) flask, at intervals varying from one to twenty-four hours following dye-administration. After an accurate determination of the hydrogen ion concentration of each specimen, samples from each were transferred to sterile test tubes, inoculated with the colon bacillus and staphylococcus albus respectively, and incubated for twenty-four hours. At the end of this period, to determine the efficiency of the dye in each sample, 0.1 cc. was transferred from each tube to melted agar and plated. Plates were inspected after another twenty-four hours. The development of an infinite number of colonies (∞) proved the corresponding urine tube to have been a suitable culture medium (fig. 1), while a sterile plate (0) indicated an efficient concentration of the dye (fig. 2).

A comparison of tables 3 and 4 demonstrates a striking influence of urinary reaction as regards dye efficiency, and is in keeping with previous experimental results shown in table 1.

TABLE 3
Alkaline urine. The secretion of antiseptic urine by man following the oral administration of proflavine and acriflavine. In this table are included only those cases in which the samples of voided urine were alkaline

PATIENT	DRUG	DOSE	SUBJECTIVE SYMPTOMS	HYDROGEN ION CONCENTRATION OF URINE SAMPLES, AS DETERMINED BY COLORIMETRIC METHOD, ON EACH SAMPLE BEFORE ANTISEPTIC TEST 7.0 = NEUTRALITY					ANTISEPTIC PROPERTIES OF URINE SAMPLES. COLUMNS BELOW INDICATE NUMBER OF COLONIES WHICH DEVELOPED IN AGAR PLATE CONTAINING 0.1 CC. URINE TRANSFERRED FROM TUBE WHICH HAD PREVIOUSLY BEEN INOCULATED AND INCUBATED TWENTY-FOUR HOURS										
				Urine obtained before drug administration	Urine obtained after drug administration					Urine obtained before drug administration		Urine obtained after drug administration							
					2 hours	4 hours	8 hours	12 hours	24 hours			2 hours	4 hours	8 hours	12 hours	24 hours			
B. E. K.	Proflavine	0.3 gram	Nausea	7.8	7.6	7.4	7.4		7.2	∞	0	0		∞	∞	0			∞
B. E. T.	Proflavine	0.2	None	6.6	7.2	5.6				∞	0	0		∞	∞	0			∞
F. O. D.	Proflavine	0.15	Nausea	6.4	5.8	7.4		7.0		∞	0	0		∞	∞	0			∞
A. M. K.	Proflavine	0.15	None	7.0	7.2	7.4		6.2	7.2	∞	0	0		∞	∞	0			∞
G. R. N.	Proflavine	0.1	Catharsis	6.8	7.0	7.0	7.0			∞	0	0		∞	0	0			∞
H. U. R.	Proflavine	0.1	Catharsis	6.0	7.0	6.0	6.0	7.2		∞	0	0		∞	0	0			∞
R. O. E.	Proflavine	0.1	None	7.4	7.2					∞	∞				∞	0			∞
D. A. S.	Proflavine	0.07	Catharsis	6.8	7.4	7.2		7.2	5.0	∞	0	0		∞	∞	0			∞
R. O. E.	Proflavine	0.05	None	7.6	7.6			7.4		∞	0			∞	∞	0			∞
H. U. R.	Proflavine	0.05	None	7.4		7.4	7.2		5.4	∞	0	0		∞	0	0			∞
R. O. E.	Proflavine	0.05	None	7.6		7.0	6.6			∞	0	0		∞	0	0			∞

TABLE 4

Acid urine. The secretion of antiseptic urine by man following the oral administration of proflavine and acriflavine. In this table are included only those cases in which the samples of voided urine were acid

PATIENT	DRUG	DOSE	SUBJECTIVE SYMPTOMS	HYDROGEN ION CONCENTRATION OF URINE SAMPLES, AS DETERMINED BY COLORIMETRIC METHOD, ON EACH SAMPLE BEFORE ANTISEPTIC TEST 7.0 = NEUTRALITY					ANTISEPTIC PROPERTIES OF URINE SAMPLES. COLUMNS BELOW INDICATE NUMBER OF COLONIES WHICH DEVELOPED IN AGAR PLATE CONTAINING 0.1 CC. URINE TRANSFERRED FROM TUBE WHICH HAD PREVIOUSLY BEEN INOCULATED AND INCUBATED TWENTY-FOUR HOURS										
				Urine obtained before drug administration	Urine obtained after drug administration					Urine obtained before drug administration		Urine obtained after drug administration							
					2 hours	4 hours	8 hours	12 hours	24 hours			2 hours	4 hours	8 hours	12 hours	24 hours			
D. A. S.	Proflavine	0.3	None	5.4	5.4	5.8	6.4			C	C	C	C	C	C				
B. E. T.	Proflavine	0.3	Nausea	5.0	5.2	6.0	6.4			C	C	C	C	C	C				
E. V. S.	Proflavine	0.3	None	6.8		5.2	5.8			C	C	C	C	C	C				
D. A. S.	Proflavine	0.3	Nausea	5.0	5.8	5.8	6.4			C	0	0	0	0	0				
H. U. N.	Proflavine	0.2	None	6.8	6.0	5.6				C	0	0	0						
N. I. M.	Proflavine	0.2	Nausea	6.6	6.2	7.4	6.8			C	0	0	0						
H. U. Y.	Proflavine	0.15	None	6.6	5.8	5.8				C	0	0	0						
M. I. R.	Proflavine	0.15	Catharsis	7.0	6.8	7.2	6.2			C	0	0	0						
B. A. Y.	Proflavine	0.1	None	5.8		6.0	6.0			C	0	0	0						
B. A. Y.	Proflavine	0.1	Catharsis	5.4		5.4	5.4			C	0	0	0						
C. O. T.	Proflavine	0.1	None	5.8		5.8	7.0			C	0	0	0						
S. T. R.	Proflavine	0.07	Catharsis	6.0	7.0	5.0				C	0	0	0						
B. E. K.	Proflavine	0.07	None	7.0	7.2	6.8	6.2			C	0	0	0						
H. E. N.	Proflavine	0.05	None	7.4		6.6	7.0			C	0	0	0						

Cases listed in table 3 were receiving sodium bicarbonate (4 grams every four hours) and only those were included in which the samples of urine were alkaline, as indicated by the columns showing hydrogen ion concentration. Attention is called to the fact that the symbol 7.0 indicates neutrality and that figures in excess of this indicate alkalinity. Those cases in which alka-

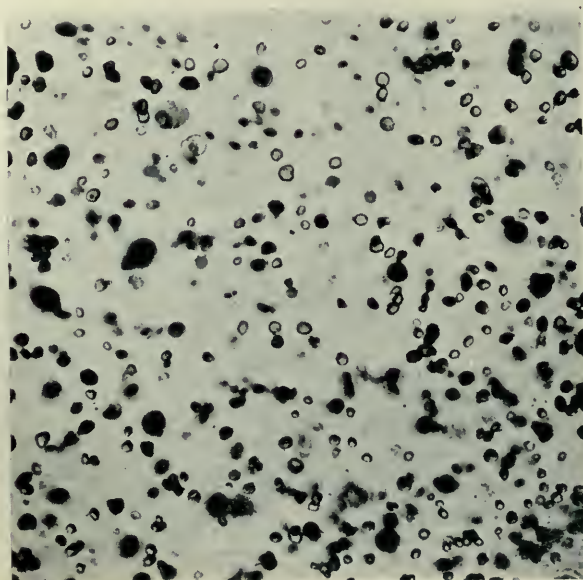


FIG. 1. URINE OBTAINED BEFORE DRUG ADMINISTRATION

Photomicrograph showing countless numbers of colonies (∞) in small area of agar plate containing 0.1 cc. of urine which had previously been inoculated and incubated for twenty-four hours.

linization failed are listed in table 4, together with cases in which the dye was administered alone, without attempt at alkalinization. The dye was given by mouth in capsules, in doses as indicated. The samples in this latter group were almost uniformly acid, in accordance with the findings of Henderson and Palmer (8), who have shown that the average reaction of normal urine is acid (pH 6.0).

The infinity sign (∞) indicates growth and development of the organism during the incubation period, and hence failure of the dye. The sign, 0. means death of the organism, hence dye efficiency. As indicated in table 3, after administration of 0.1 gram of either proflavine or acriflavine, in no instance did the urine obtained eight hours later fail to kill both colon bacillus



FIG. 2. URINE OBTAINED FOUR HOURS AFTER DRUG ADMINISTRATION

Photomicrograph showing complete absence of colonies in agar plate containing 0.1 cc. of urine which had previously been inoculated and incubated for twenty-four hours. Contrast with figure 1.

and staphylococcus. After this dose, in one instance only did the four-hour specimen fail to kill the colon bacillus. The specimen obtained 2 hours after drug administration failed to kill the organisms 3 times out of 14. The samples of acid urine in table 4, however, almost uniformly permitted the growth of the colon bacillus, occasionally killing the staphylococcus. This is in keeping with the relative resistance of the two organisms as demonstrated in table 1.

Tables 3 and 4 permit the conclusion that staphylococci and colon bacilli, introduced into (alkaline) urine obtained after drug administration, die at some time during the twenty-four hour incubation period, while those organisms in the control samples of urine grow and develop.

To determine the length of time which these organisms survive in dye-containing (alkaline) urine, 10 cc. samples of urine,

TABLE 5

The rate of death of colon bacilli in urine obtained after the oral administration of proflavine and acriflavine

PATIENT, DRUG AND DOSE	SAMPLES OF URINE OB- TAINED BE- FORE, AND FOUR HOURS AFTER DRUG ADMINISTRA- TION	H-ION CONCENTRATION	FIGURES INDICATE APPROXIMATE NUMBER OF COLONIES WHICH DEVELOPED IN AGAR PLATES, EACH CONTAINING 0.1 CC. OF URINE TRANSFERRED AT INTERVALS FROM TUBES CONTAINING URINE OBTAINED BEFORE AND AFTER DRUG ADMINISTRATION						
			Plate poured before inocu- lation	Plates poured at intervals after inoculation					
				Imme- diate	1 hour	2 hours	4 hours	8 hours	24 hours
H. U. R., pro- flavine, 0.05 gram	Before	7.4	0	1,000	1,000	1,000	1,000	∞	∞
	After	7.4	0	1,000	1,000	50	10	0	0
R. O. E., pro- flavine, 0.5 gram	Before	7.6	0	1,000		10,000	10,000	∞	∞
	After	7.4	0	1,000	1,000	1,000	500	100	0
B. A. Y., acri- flavine, 0.05 gram	Before	6.8	0	1,000		10,000		∞	∞
	After	7.6	0	1,000		1,000		0	0

10 cc. samples of urine were each inoculated with one loop of a twenty-four hour culture of the colon bacillus, and placed in the incubator. 0.1 cc. amounts were plated at intervals, as indicated above.

0 = No colonies; ∞ = an infinite number of colonies.

passed by patients after dye administration, were inoculated with colon bacilli and placed in the incubator. From these samples, at intervals of one to several hours, 0.1 cc. amounts were plated. With each experiment, as a control, was used a sample of urine obtained before dye administration from the same patient, and subjected to identically the same conditions. A study of table 5 shows that in the dye-containing urine the

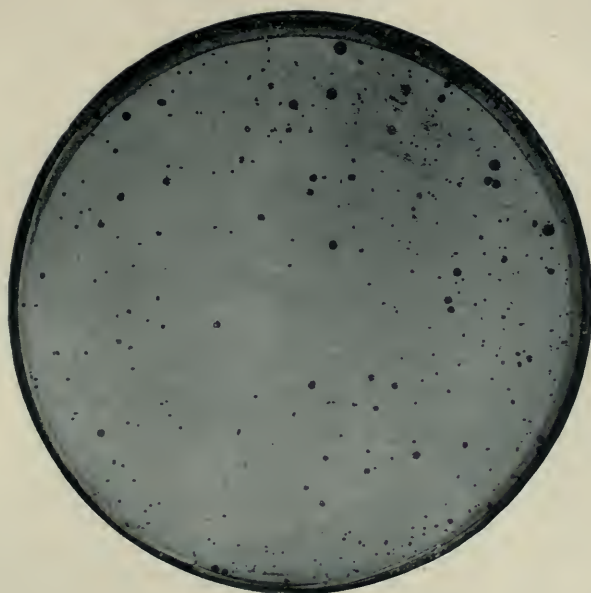


FIG. 3. PLATE POURED IMMEDIATELY AFTER INOCULATION

Photograph showing numerous colonies in agar plate containing 0.1 cc. of urine transferred from a specimen obtained four hours after administration of acriflavine (0.05 gram) and inoculated with colon bacilli.



FIG. 4. PLATE POURED EIGHT HOURS AFTER INOCULATION

Photograph showing complete absence of colonies in agar plate, containing same amount of urine transferred from same specimen mentioned in description of figure 3.

number of organisms gradually diminishes through about eight hours to zero, while in the control rapid development takes place. Attention is called to the fact that the dosage producing these results was exceedingly minute (0.05 gram). The death of colon bacilli within eight hours in dye-containing urine is illustrated by contrasting figures 3 and 4, which are photographs of agar plates, each containing 0.1 cc. of urine transferred from the same tube, one immediately after inoculation (fig. 3) and the other eight hours later (fig. 4).

CLINICAL CONSIDERATIONS

It is to be particularly noted that the data here presented was obtained by the administration of these dyes to *normal* individuals. The results are, therefore, purely experimental in character, and in no way clinical, in that the effect (if any) of the acridin dyes upon existing pathological conditions awaits demonstration. Clinical experience to date is too meagre to form the basis of an opinion.

If clinically efficient, these dyes should find their particular field of usefulness in any acute or chronic inflammatory condition of the urinary tract, *not dependent upon* some accessory cause for infection, such as retention, stone, tumor or tuberculosis. The most enthusiastic advocate of drug therapy could not expect therapeutic results until all the underlying causes for persistent infection have been excluded by accurate diagnosis, or eliminated by surgical measures where indicated. No conceivable drug could be expected to relieve the cystitis resulting from carcinoma, or stone, or from prostatic retention.

In particular, the ideal internal urinary antiseptic should be of value in the treatment of uncomplicated, chronic pyelitis of adults, in pyelitis of infancy, in acute pyelonephritis and cystitis, and in the chronic bacteriurias, including those due to typhoid bacilli, colon bacilli and staphylococci. It should be of value also as a prophylactic following urethral or ureteral instrumentation.

Attention has been called to the high dilution (1:300,000) in which acriflavine inhibits the gonococcus (Davis and Harrell (8)).

Given in minimum dosage, the concentration of acriflavine in the urine is such that the few drops following urination stain fabrics a deep yellow. There has been made no quantitative estimation of the amount appearing in the urine, but the drug is evident in no other excretion, and is probably completely eliminated by the kidney. Assuming that only half of a 0.1 gram dose appears in the urine during twenty-four hours, a very simple estimation shows that the concentration in the urine is far in excess of that necessary to inhibit the gonococcus. Therefore, in the treatment of gonorrhea, acriflavine, administered internally, should theoretically be of value for the following purposes:

1. As a prophylactic.
2. In the treatment of early anterior urethritis.
3. To prevent the development of posterior urethritis.
4. In the treatment of early posterior urethritis.

In a very limited number of cases, favorable results have been obtained in both anterior and posterior infections of recent date. In each case, however, after a very brief period of observation, it was considered advisable to supplement this treatment by urethral instillations of acriflavine, in order not to deprive the patient of the benefit of early local treatment.

SUMMARY

There is no sound experimental or clinical proof of the fitness of any known drug for use as an internal urinary antiseptic.

Proflavine and acriflavine, administered by mouth in 0.1 gram and even 0.05 dosage; to normal individuals is secreted in the urine in sufficient concentration to render the latter an unfit culture medium for the colon bacillus and staphylococcus, *provided the reaction of the urine is alkaline*. The same effect is inconstantly obtained in acid urine. This antiseptic action becomes evident about two hours after drug-administration, and persists for at least eight hours. Control samples of urine, obtained before drug-administration and twenty-four hours later, uniformly permitted a profuse growth of both organisms.

Colon bacilli survive for only about eight hours in dye-containing *alkaline* urine, as determined by interval cultures from inoculated, incubated urine, obtained from patients four hours after the administration of acriflavine, or proflavine, 0.05 gram.

Preliminary experiments indicate that intravenous administration of smaller dosage causes more prompt and efficient antiseptic action.

While there are certain definite toxic limits (as yet undetermined), rabbits have survived, with no apparent ill-effect, a daily dosage for thirty days of one-half the *actual* (not relative) antiseptis-producing dose given to man. This amount given to rabbits was 0.01 gram per kilo, or approximately 0.025 gram daily.

It is not conceivable that even the ideal internal urinary antiseptic could be expected to have a beneficial effect upon urinary infections secondary to some underlying cause, such as stone, tumor or retention. Therefore, in no instance is it advisable to substitute promiscuous medication for systematic accurate diagnosis, and operative measures where indicated.

No claims whatever are made for clinical results following the internal administration of these dyes. The indiscriminate use for this purpose of products marketed under the name of proflavine or acriflavine, but of undetermined purity and toxicity and efficiency is distinctly inadvisable.

Experimentally, however, the above results constitute a distinct step forward, in demonstrating the hitherto theoretical possibilities offered by the anilin dyes. There has heretofore appeared in the literature no conclusive proof (dependent upon exact cultural methods) of antiseptic properties of human urine resulting from drug administration. Clinical investigation of proflavine and acriflavine, and experimental investigation of related compounds, is therefore clearly indicated.

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THE ACTION ON THE GONOCOCCUS OF VARIOUS DRUGS COMMONLY USED IN THE PROPHYLAXIS AND TREATMENT OF GONORRHEA

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and Cure of Venereal Diseases*

I. INTRODUCTION

In the course of a series of researches on venereal disease, we have developed a method for testing the germicidal activity of drugs against the gonococcus, which offers advantages over those previously used. In a paper upon this method (1) we have discussed the theoretical considerations underlying it. In order to compare the results obtained by this method in the case of new drugs developed in this laboratory with those commonly in use, we have performed a series of experiments using a number of drugs commonly employed in the prophylaxis and treatment of gonorrhea, as well as potassium mercuric iodide and chlorazene, which are general disinfectants. In this paper we desire to present the results of this series.

II. HISTORICAL

Schaefer and Steinschneider (1894) (2) used a method in which gonococci were suspended in a mixture of 2 parts distilled water and 1 part human serum heated one-half hour to 60°C. After the emulsion had remained in contact with the test-drug, the desired time at 35°C., 3 loops were transferred to serum agar. They found that phenol in dilutions of 1:20, 1:40 or 1:100 would kill gonococci in five minutes, and that potassium permanganate 1:1000, boric acid 1:100, zinc sulphate 1:400, and

tannic acid 1:50 did not kill in fifteen minutes. Their best results were obtained with aethylene diamine silver phosphate, a drug not now used in this country, which killed at 1:2000 in five minutes. Culver (1917) (3), tested silver compounds by mixing them with emulsions of gonococci, and at the end of specified times, removing one drop of the mixture which was spread upon slanted blood agar. His results are as follows: Argyrol, 1 per cent kills at once, 0.5 per cent in five minutes, 0.25 per cent in ten minutes, and 0.125 per cent in thirty minutes. Protargol, 0.25 per cent at once, 0.125 per cent in ten minutes, 0.03125 per cent in thirty minutes. Silvol, 0.5 per cent at once, 0.25 per cent in ten minutes, 0.03125 per cent in thirty minutes. Nargol, 0.25 per cent at once, 0.0625 per cent in ten minutes, 0.03125 per cent in thirty minutes. He showed that the silver compounds lose germicidal power as the result of standing or heating, and also felt that he had demonstrated that gonococci acquire a resistance to the silver compounds after long growth in weak concentrations.

Post and Nicoll (1910) (4) tested many germicides by a method in which one loopful of the organism was placed in 0.5 cc. of a solution of the test drug. At the end of the test period, one loopful of the drug-organism mixture was transferred to blood-agar and plated. The temperature of the reaction is not stated. According to them, argyrol 50 per cent fails to kill gonococci in less than twenty hours, while protargol 10 per cent kills in ten minutes. Weaker solutions failed to kill. Potassium mercuric iodide, combined with sodium bicarbonate, in the form of a proprietary preparation known as "germicidal discs" killed at a concentration of 1:1156 (calculated for the double salt) in one minute, and failed to kill at 1:2890 in thirty minutes. Trikresol 1 per cent killed in one minute, phenol 1 per cent in thirty minutes, and permanganate of potassium 1:4000 in thirty minutes. Zinc sulphate 1:500 failed to kill in thirty minutes. Gonococci grew well after being placed in distilled water for twenty hours. This last result, and that for argyrol 50 per cent do not correspond with the experience of ourselves or others with the gonococcus.

Clark and Wylie (1911) (5) mixed 2 cc. of an emulsion of gonococcus with 2 cc. of a solution of the test-drug. At the end of five, fifteen and thirty minutes, one loopful was transferred to ascitic fluid agar and plated. Their results are that argyrol 30 per cent, collargol 2.5 per cent and protargol 10 per cent did not kill in thirty minutes, while cargeritos 20 per cent killed in thirty minutes.

Furstenau (1918) (6) transferred with a loop from drug-organism mixtures at the end of stated periods. The results obtained are: Zibosal kills at 1:40 in two and one-half minutes, 1:400 in ten minutes. Albargin at 1:400 in two and one-half minutes. Syrgol at 1:400 in two and one half minutes, 1:4000 in ten minutes. Collargol at 1:400 in two and one-half minutes. Sophol at 1:4000 in two and one-half minutes. Choleval at 1:400 in two and one-half minutes. Most of these drugs are not familiar in this country, but some of them at least are silver compounds probably similar to those used here.

It is evident from the results of these workers that the silver compounds have a definite activity against the gonococcus, while permanganate, zinc sulphate and boric acid have shown no such activity. The present article covers a number of classes of compounds, all tested by the same method, so that comparisons between them may be made.

III. METHOD

The method used was that described in the article referred to above (1). Briefly, it is as follows:

One cubic centimeter of the emulsion is pipetted into a centrifuge tube of diluted drug. The tube is placed in the water bath at 37.5°C. for eighteen minutes. At the end of this time, it is centrifuged at high speed for two minutes. The supernatant fluid is poured off, and a quantity of salt solution pipetted in. This makes the complete time of action of the drug twenty minutes. The tube is then spun a second time, and the wash fluid poured off. The gonococci settle readily in the centrifuge, and form a compact mass at the tip of the tube, which can be transferred almost en masse to a tube of fresh media. This is corked

and incubated, as described by Swartz (7). It is our custom to inoculate, after seven days, all tubes, upon which no growth has occurred, with fresh cultures of gonococci. If they develop, we assume that enough of the drug has not been carried over to the test medium to prevent growth. All final growths are examined microscopically, with the Gram stain.

IV. RESULTS

The results are presented in the form of tables. For each substance, a typical experiment is given. Checks have shown that the end-points given are constant. Suitable controls were made in each experiment.

The solutions of the silver compounds and chlorazene were made freshly before each experiment from material purchased in the open market. Phenol, potassium permanganate, zinc sulphate and boric acid solutions were made from the chemically pure drugs in the laboratory. The tricresols used were a sample of a product redistilled between 195° and 205°C. furnished by Dr. R. T. Devereaux of the Mulford Company, to whom we are much indebted. The sample was about two months old, had been kept in the cold in a brown glass bottle, and showed only a very slight brownish discoloration. The potassium mercuric iodide solutions were made in the laboratory by dissolving mercuric iodide in a solution of potassium iodide. The dilutions given are calculated on the content of the double salt. A slight excess of potassium iodide must be present to keep the double salt in solution.

Table 12 shows the end-points obtained for each of the drugs in the series.

Tables 13 to 18 inclusive show the results of some experiments performed to determine the resistance of common laboratory organisms to the same drugs by the same technique. This technique would be expected to show low germicidal values, since large quantities of organisms are used, and large numbers are transferred to the culture media.

TABLE 1

Silvol

GONOCOCCUS	STRENGTH OF SOLUTIONS										CONTROLS	
	1:100	1:200	1:400	1:800	1:1000	1:1200	1:1600	1:2000	1:3200	1:6400	H ₂ O	NaCl
24-hour reading.....	0	0	0	0	0	0	+	+	+	+	+	+
48-hour reading.....	0	0	0	+	+	0	+	+	+	+	+	+
7-day reading.....	0	0	0	+	+	0	+	+	+	+	+	+
Tubes reinoculated.....	✓	✓	✓									
24-hour reading.....	+	+	+									
48-hour reading.....	+	+	+									

* One colony.

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 2

Cargentos

GONOCOCCUS	STRENGTH OF SOLUTION					CONTROLS	
	1:400	1:800	1:1600	1:3200	1:6400	H ₂ O	NaCl
24-hour reading.....	0	0	+	+	+	+	+
48-hour reading.....	0	0	+	+	+	+	+
7-day reading.....	0	0	+	+	+	+	+
Tubes reinoculated.....	✓	✓					
24-hour reading.....	+	+					
48-hour reading.....	+	+					

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 3

Argyrol

GONOCOCCUS	STRENGTH OF SOLUTIONS						CONTROLS	
	1:400	1:800	1:1600	1:3200	1:6400	1:12800	NaCl	H ₂ O
24-hour reading.....	0	0	+	+	+	+	+	+
48-hour reading.....	0	0	+	+	+	+	+	+
7-day reading.....	0	0	+	+	+	+	+	+
Tubes inoculated.....	✓	✓						
24-hour reading.....	+	+						
48-hour reading.....	+	+						

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 4
Protargol

GONOCOCCUS	STRENGTH OF SOLUTIONS							CONTROLS	
	1: 100	1: 200	1: 400	1: 800	1: 1600	1: 3200	1: 6400	H ₂ O	NaCl
24-hour reading....	0	0	0	+	+	+	+	+	+
48-hour reading....	0	0	0	+	+	+	+	+	+
7-day reading.....	0	0	0	+	+	+	+	+	+
Tubes inoculated..	✓	✓	✓						
24-hour reading....	+	+	+						
48-hour reading....	+	+	+						

C = Control tube.
 + = Growth of gonococcus.
 0 = No growth of gonococcus.

TABLE 5
Phenol

GONOCOCCUS	STRENGTH OF SOLUTIONS									CONTROLS	
	1: 50	1: 100	1: 200	1: 400	1: 800	1: 1600	1: 3200	1: 6400	1: 12800	H ₂ O	NaCl
24-hour reading.....	0	0	0	+	+	+	+	+	+	+	+
48-hour reading.....	0	0	0	+	+	+	+	+	+	+	+
7-day reading.....	0	0	0	+	+	+	+	+	+	+	+
Tubes inoculated.....	✓	✓	✓								
24-hour reading.....	+	+	+								
48-hour reading.....	+	+	+								

C = Control tube.
 + = Growth of gonococcus.
 0 = No growth of gonococcus.

TABLE 6
Tricresols

GONOCOCCUS	STRENGTH OF SOLUTIONS							CONTROLS	
	1: 200	1: 400	1: 800	1: 1600	1: 3200	1: 6400	1: 12800	H ₂ O	NaCl
24-hour reading....	0	0	0	+	+	+	+	+	+
48-hour reading....	0	0	0	+	+	+	+	+	+
7-day reading.....	0	0	0	+	+	+	+	+	+
Tubes inoculated..	✓	✓	✓						
24-hour reading....	+	+	+						
48-hour reading....	+	+	+						

C = Control tube.
 + = Growth of gonococcus.
 0 = No growth of gonococcus.

TABLE 7
Potassium permanganate

GONOCOCCUS	STRENGTH OF SOLUTIONS							CONTROLS	
	1: 1000	1: 2000	1: 4000	1: 8000	1: 16000	1: 32000	1: 64000	NaCl	H ₂ O
24-hour reading	0	0	0	+	+	+	+	+	+
48-hour reading	0	0	0	+	+	+	+	+	+
7-day reading	0	0	+	+	+	+	+	+	+
Tubes inoculated ..	✓	✓							
24-hour reading	+	+							
48-hour reading	+	+							

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 8
Zinc sulphate

GONOCOCCUS	STRENGTH OF SOLUTIONS							CONTROLS	
	1: 100	1: 200	1: 400	1: 800	1: 1600	1: 3200	1: 6400	H ₂ O	NaCl
24-hour reading	0	0	0	0	+	+	+	+	+
48-hour reading	+	+	+	+	+	+	+	+	+
7-day reading									
Tubes inoculated ..									
24-hour reading									
48-hour reading									

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 9
Boric acid

GONOCOCCUS	STRENGTH OF SOLUTIONS									CONTROLS	
	1: 50	1: 83	1: 100	1: 125	1: 166	1: 250	1: 500	1: 1250	1: 2500	H ₂ O	NaCl
24-hour reading	+	+	+	+	+	+	+	+	+	+	+
48-hour reading	+	+	+	+	+	+	+	+	+	+	+
7-day reading											
Tubes inoculated											
24-hour reading											
48-hour reading											

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 10
Potassium mercuric iodide

GONOCOCCUS	STRENGTH OF SOLUTIONS								CONTROLS	
	1:5000	1:10,000	1:20,000	1:40,000	1:80,000	1:160,000	1:320,000	1:640,000	H ₂ O	NaCl
24-hour reading	0	0	0	0	0	+	+	+	+	+
48-hour reading	0	0	0	0	0	+	+	+	+	+
7-day reading	0	0	0	0	0	+	+	+	+	+
Tubes inoculated	✓	✓	✓	✓	✓					
24-hour reading	+	+	+	+	+					
48-hour reading	+	+	+	+	+					

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 11
Chlorazene

GONOCOCCUS	STRENGTH OF SOLUTIONS								CONTROLS	
	1:100	1:200	1:400	1:800	1:1600	1:3200	1:6400	1:12800	H ₂ O	NaCl
24-hour reading	0	0	0	0	0	0	+	+	+	+
48-hour reading	0	0	0	0	0	0	+	+	+	+
7-day reading	0	0	0	0	0	0	+	+	+	+
Tubes inoculated	✓	✓	✓	✓	✓	✓				
24-hour reading	+	+	+	+	+	+				
48-hour reading	+	+	+	+	+	+				

C = Control tube.

+ = Growth of gonococcus.

0 = No growth of gonococcus.

TABLE 12

SOLUTION	IN TWENTY MINUTES	
	Gonococcus killed at	Gonococcus grows at
Silvol.....	1:400	1:800
Cargentos.....	1:800	1:1600
Argyrol.....	1:800	1:1600
Protargol.....	1:400	1:800
Phenol.....	1:200	1:400
Tricresols.....	1:800	1:1600
Potassium permanganate.....	1:2000	1:4000
Zinc sulphate.....		1:100
Boric acid.....		1:50
Potassium mercuric iodide.....	1:40000	1:80000
Chlorazene.....	1:3200	1:6400

TABLE 13

Silvol

B. COLI	STRENGTH OF SOLUTIONS						CONTROLS	
	1:10	1:20	1:100	1:200	1:400	1:800	H ₂ O	NaCl
24-hour reading.....	+	+	+	+	+	+	+	+
48-hour reading.....	+	+	+	+	+	+	+	+
7-day reading.....	+	+	+	+	+	+	+	+
Tubes inoculated.....								
24-hour reading.....								
48-hour reading.....								

C = Control tube.

+ = Growth of *B. coli*.0 = No growth of *B. coli*.

TABLE 14

Silvol

STAPHYLOCOCCUS	STRENGTH OF SOLUTIONS						CONTROLS	
	1:10	1:20	1:100	1:200	1:400	1:800	H ₂ O	NaCl
24-hour reading.....	+	+	+	+	+	+	+	+
48-hour reading.....	+	+	+	+	+	+	+	+
7-day reading.....	+	+	+	+	+	+	+	+
Tubes inoculated.....								
24-hour reading.....								
48-hour reading.....								

C = Control tube.

+ = Growth of staphylococcus.

0 = No growth of staphylococcus.

TABLE 15

Phenol

B. COLI.	STRENGTH OF SOLUTIONS						CONTROLS	
	1:50	1:100	1:200	1:400	1:800	1:1600	H ₂ O	NaCl
24-hour reading	+	+	+	+	+	+	+	+
48-hour reading	+	+	+	+	+	+	+	+
7-day reading	+	+	+	+	+	+	+	+
Tubes inoculated								
24-hour reading								
48-hour reading								

C = Control tube.

+ = Growth of *B. coli*.0 = No growth of *B. coli*.

TABLE 16

Phenol

STAPHYLOCOCCUS	STRENGTH OF SOLUTIONS						CONTROLS	
	1:50	1:100	1:200	1:400	1:800	1:1600	H ₂ O	NaCl
24-hour reading	+*	+	+	+	+	+	+	+
48-hour reading	+	+	+	+	+	+	+	+
7-day reading	+	+	+	+	+	+	+	+
Tubes inoculated								
24-hour reading								
48-hour reading								

* 25 colonies.

C = Control tube.

+ = Growth of *staphylococcus*.0 = No growth of *staphylococcus*.

TABLE 17

Potassium mercuric iodide

B. COLI.	STRENGTH OF SOLUTIONS							CONTROLS	
	1:100	1:200	1:400	1:800	1:1600	1:3200	1:6400	H ₂ O	NaCl
24-hour reading	0	0	0	0	0	0	0	+	+
48-hour reading	0	0	0	0	0	+	0	+	+
7-day reading									
Tubes inoculated . . .									
24-hour reading									
48-hour reading									

C = Control tube.

+ = Growth of *B. coli*.0 = No growth of *B. coli*.

TABLE 13
Potassium mercuric iodide

STAPHYLOCOCCUS	STRENGTH OF SOLUTIONS							CONTROLS	
	1:100	1:200	1:400	1:800	1:1600	1:3200	1:6400	H ₂ O	NaCl
24-hour reading	0	0	0	0	0	+	0	+	+
48-hour reading									
3-day reading	0	+8*	0	+5*	+50*	+150*	+	+	+
Tubes inoculated ..									
24-hour reading									
48-hour reading									

* The figures represent the number of colonies.

C = Control tube.

+ = Growth of staphylococcus.

0 = No growth of staphylococcus.

V. DISCUSSION

The four silver compounds tested all show about the same germicidal power for the gonococcus. The figures obtained are not irreconcilable with those of Culver (3) and Schaffer and Steinschneider (2). Phenol is not used in the treatment of gonorrhea, but has been employed as a prophylactic. Its activity against the gonococcus is slight, and it will not kill in twenty minutes in any strength in which it may be used in the urethra in a water solution. The tricresols are about four times as active as pure phenol. Potassium permanganate solutions up to a strength of about 1:16,000 are completely decolorized by the gonococcus emulsion during the test-period of twenty minutes. The stronger solutions retain a pink tinge. It kills at 1:2000, while at 1:4000, the strongest solution used in the urethra fails to kill in twenty minutes. Zinc sulphate and boric acid do not kill in any strength employed. Potassium mercuric iodide stands out from all the others in killing at a dilution of 1:40,000 in twenty minutes. As far as we are aware, this drug has not been used in the treatment of gonorrhea. A few tests made indicate that it can be tolerated in the urethra without symptoms of irritation in a strength of 1:200.

Chlorazene surpasses the other drugs except the potassium mercuric iodide, and is lethal for gonococci in twenty minutes

well within the therapeutic range. Some observers have had good results with chlorazene in the treatment of gonorrhea, but it has not come into general use on account of its irritating properties.

In another paper (1), we have suggested a factor to indicate roughly the probable usefulness of germicidal drugs. This factor is obtained by dividing the concentration in which a drug will kill gonococci in twenty minutes by the concentration in which it may be used in the urethra. For the drugs in this series, factors may be calculated as follows:

DRUG	KILLS AT	MAY BE USED AT	FACTOR
Silvol.....	1:400	1:4	100
Cargentos.....	1:800	1:4	200
Argyrol.....	1:800	1:6.6	121
Protargol.....	1:400	1:50	8
Potassium permanganate.....	1:2000	1:4000	0.5
Potassium mercuric iodide.....	1:40000	1:200	200
Chlorazene.....	1:3200	1:400	8

It will be seen that a factor of less than unity indicates that the drug will not kill in any concentration in which it may be used in the urethra. At the present time, we cannot say what relation exists between this factor and therapeutic value. It will be noted that the silver compounds have large factors, due to the great concentration in which they may be used without irritation. We are dealing, in their case, however, with colloidal suspensions, the penetrating power of which is undoubtedly less than that of true solutions of easily diffusible substances, such as Mercurochrome-220 and the flavines. Therefore, the factor would have to be modified further to serve as an exact guide to therapeutic usefulness, and is but a rough means of comparing new drugs as to their probable activity in actual use.

It is likely that a field of usefulness in the urethra is open to such a drug as potassium mercuric iodide as a therapeutic or prophylactic agent. Its great superiority as a germicide to the silver preparations and to other drugs in common use, together with its property of not precipitating protein, should earn for

it serious consideration. Its germicidal activity is inferior only to a few new drugs of the Mercurochrome series, the results with which are being published in another paper.

The results with *B. coli* and staphylococcus by the same technique indicate clearly that for the drugs used, the gonococcus is very much more susceptible than these common organisms. The concentration of potassium mercuric iodide necessary to kill *B. coli* is roughly 25 times as strong as that required to kill gonococcus, and for staphylococcus 100 to 200 times as strong. These figures correspond with others obtained by us for other drugs. Steinschneider and Schaffer called attention to the unexpectedly high resistance shown by the gonococcus in their tests. Our results show that while the gonococcus has a definite resistance to drugs and other deleterious agents, enabling it to be handled with freedom and certainty, this resistance is of a much lower order than that shown by such organisms as *B. coli* and *S. aureus*.

VI. CONCLUSIONS

1. Silvol, cargentos, argyrol and protargol have a definite but not very high germicidal value against the gonococcus. For all these substances the values are of the same order.

2. Phenol, tricresols, potassium permanganate, zinc sulphate and boric acid have too little germicidal value against the gonococcus to be useful as germicides in the urethra.

3. Chlorazene has a moderate germicidal value against the gonococcus.

4. Potassium mercuric iodide has a high germicidal value against the gonococcus.

5. The gonococcus is many times more susceptible to the drugs tested than are *B. coli* or *S. aureus*.

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SUBMUCOUS ULCER OF THE BLADDER IN THE MALE

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Operations have been performed in the Mayo Clinic since December 1, 1916, in fifteen cases of submucous ulcer of the bladder. Two of these cases occurred in the male. In Hunner's initial article on this subject he used the title "Rare form of bladder ulcer" and contrasted the condition with the simple ulcer described by Fenwick. Since then several descriptive terms have been suggested for the infection; Cullen offered "Elusive ulcer" because of its difficulty of diagnosis. Geraghty proposed "Paracystitis" and more recently Keene proposed the comprehensive and inclusive term of "Pan mural ulcerative cystitis." The term "submucous ulcer" is one that has been in use in the Mayo Clinic since the condition was first recognized.

Because the disease only slightly involves the mucosa and greatly involves the submucosal structure, the term seems to be concise and descriptive and to differentiate clearly the condition found from that of simple ulcers of the bladder in which the destruction is largely of the mucosa.

Although the etiology of the disease has remained in obscurity, there is nothing concerning it to indicate that it is confined to the female. Diseases of the female pelvic organs and pregnancy are apparently in no way associated with its onset. Since the practice of the physician who originally described the condition was confined to women he had not, obviously, observed cases in the male. He stated, however, that he believed the condition would be found in the male. A careful search of the literature, however, fails to reveal any reported cases in the male.

Focal infection has often been suggested as a cause of the condition but from the clinical side alone proof of this has not been possible. The fact that the disease occurs in young adults

(the average age in our series was thirty-two at the time of onset) has been considered suggestive.

The condition indicates a blood born infection. The blood vessels are prominent, and as brought out by Keene polymorphonuclear leukocytes are seen not only within the lumen but infiltrating the vessel walls and paravesical tissues. There is also a marked diffuse submucous lymphocytic infiltration which together with the extravasation of the red blood cells through the surrounding tissue is added evidence of the infective origin of the lesion. The perivascular changes, cellular infiltration and edema are usually most marked in the outer coats of the bladder. The mucosa frequently shows but slight involvement; the infection evidently is not carried by the urine since the tissues in contact with it are the least involved.

Eight of the fifteen patients showed periapical infection in their dental roentgenograms. Often many teeth were abscessed, a fact that lead to experimental studies which resulted in demonstrating that from such areas of dental infection bacteria are obtainable. These bacteria, injected into laboratory animals, show elective affinity for the bladder and produce similar lesions in the bladders of the animals. The fact that the condition has been reported more frequently in the female remains unexplained. The two male cases here reported demonstrate that in this sex at least Cullen's term of "Elusive ulcer" is still applicable.

The fact that an extensive pathologic process may occur in the bladder without producing changes in the urine, which are suggestive of the disease, has probably been a most potent factor in preventing the early diagnosis of the condition.

In both cases here reported the microscopic examination of the urine was negative as it was in eight others of the series. Yet both patients gave a history of intermittent attacks of gross hematuria in the past, as did the other thirteen of the series. Such hematuria has been noted by various observers and is explained by the ease with which the ulcer area can be made to bleed either by overdistension or by trauma; a condition frequently noted during cystoscopic examination and undoubtedly occurring when external pressure or long retention have occurred, which have produced the gross hematuria noted.

Such findings associated with a history of pain and frequency of equal severity by day and by night are pathognomonic of the disease; both of the male patients gave such a history.

In all of the cases in the series the first bladder symptoms dated back eight years, the average was ten years. This illustrates quite as graphically as the numerous operations to which such patients are needlessly subjected how infrequently the disease is recognized.

Submucous ulcers of the bladder

	CASES	AGE AT ONSET	SEX	PREGNANCIES	TONSILLITIS	GRIPPE	RHEUMATISM	ABSCESSSED TEETH	DURATION OF DISEASE-YEARS	GROSS HEMATURIA	OCCASIONAL RED BLOOD CELLS	OCCASIONAL PUS CELLS	DATE OF OPERATION	CURED
1	168286	33	F	0	+	-	-	-	3	+	+	0	12- 6-1916	+
2	221983	36	F	0	+	-	+	+	8	+	0	0	3- 2-1918	0
3	224017	26	F	2	+	-	-	+	30	-	-	-	3-25-1918	+
4	222836	31	F	1	-	-	-	+	8	+	+	+	4-20-1918	-
5	245776	27	F	1	-	+	+	-	9	-	0	+	10- 2-1918	0
6	247241	45	F	0	-	-	-	-	6	+	+	+	10-17-1918	0
7	255187	44	F	2	-	-	-	0	5	+	0	0	1-21-1919	0
8	255950	39	F	2	-	+	-	+	8	+	0	0	1-21-1919	+
9	18196	25	M	-	-	+	-	+	11	+	0	0	3-28-1919	-
10	299174	24	F	2	-	-	-	+	7	+	0	0	3-22-1920	+
11	314926	22	M	-	-	-	-	-	8	+	0	0	6- 3-1920	-
12	93637	33	F	1	+	-	-	+	21	+	0	0	10- 8-1920	-
13	340270	50	F	1	+	+	-	-	8	+	0	+	12-21-1920	-
14	52145	26	F	3	+	-	-	+	9	+	0	0	1-24-1921	-
15	348635	28	F	1	+	+	-	0	8	+	+	+	2-15-1921	-

We have records of eight of ten patients operated on more than one year. Four report complete cures, the other four no improvement. It has frequently been noted that when resection does result in cure it brings immediate relief. If this does not occur, inquiries bring the statement that the condition is unchanged; to be worse than before operation seems impossible. We believe that the high percentage of poor results may be due to the recurrence of the condition because of remaining foci. We are attempting to have such patients return and to have all foci removed, although it cannot be stated that the removal of the foci alone will always result in cure. We have two patients

under observation who are opposed to surgery and are awaiting the results of eradication of foci. The bacteria from the teeth of both patients showed local affinity for the bladder when injected into laboratory animals.

REPORTS OF TWO CASES OCCURRING IN THE MALE

Case 18196. Mr. J. N., aged twenty-five, first registered at the Clinic December 18, 1908. He complained of having had occasional cramps in the right abdomen for four years, lasting from ten to fifteen minutes, with marked soreness in the right lower quadrant during the past month. He had noticed some frequency and slight dysuria.

Cystoscopic examination and roentgenograms of the urinary tract were negative; the specific gravity of the urine was 1015, the reaction was acid; there was a faint trace of albumin, no sugar, and a few hyalin and granular casts.

December 28 1908, an acute perinephritic abscess was drained and a chronic appendix removed.

The patient returned to the Clinic eight years later, 1916, stating that his bladder condition had never improved and that he still had a day frequency of from six to eight and a nocturia of three or four, associated with sharp pain in the bladder when it was distended. Occasionally he felt burning but he had never seen blood or gravel. With the bladder full he experienced slight incontinence.

The physical examination was negative except for slight suprapubic tenderness. The urinalysis, urine culture, roentgenograms of the urinary tract, and cystoscopic examination were negative. The patient was discharged.

Three years later the patient returned again complaining as before but with symptoms more severe; frequency was increased and incontinence with a full bladder was so much increased that he often wet his bed. His health otherwise was good.

Urinalyses and roentgenograms still remained negative, but cystoscopic examination revealed an area of increased reddening and edema in the posterior wall of the bladder near the dome; the vessels radiating from it were engorged. The remainder of the bladder was negative. The clinical symptoms and the cystoscopic findings all corresponded to the type of ulcer described by Hunner in the female. The diagnosis of submucous ulcer of the bladder was made, and after the usual attempts at treatment by lavage, and so forth, the edematous area was resected March 28, 1919. The pathologist reported "Very marked

submucous lymphocytic infiltration, extravasation of blood, epithelium markedly thinned (Hunner ulcer)."

Case 319426. Mr. F. H., aged thirty, registered in the Clinic May 6, 1920. He complained of dysuria and stated that eight years before he had been sick for three months with ulcers of the bladder. He had had at that time marked frequency, and hematuria. He apparently completely recovered and had no further symptoms until the onset of the present trouble five years before. He had sharp and very severe pain in the urethra lasting about half an hour, and was relieved by voiding. For the first few years this pain occurred at long intervals but for the last three months it occurred every day and was associated with a day frequency of twelve and a nocturia of four or five. He also had a deep perineal pain, most extreme just before voiding. This disappeared immediately on urination.

The urinalysis showed a specific gravity of 1010, acid reaction, slight trace of albumin, no sugar, and an occasional red blood cell. Roentgenograms of the urinary tract were negative. Cystoscopic examination showed an irregular, edematous area about 2 cm. in diameter in the dome of the bladder. This corresponded in appearance to the ulcers described by Hunner. Specimens of urine from both kidneys were negative. A diagnosis of submucous ulcer was made.

June 3, the bladder was opened. In the dome in the left side was found the area described. The bladder wall at this point was definitely thickened and seemed to be edematous. The mucous membrane was reddened and the peritoneum attached so that it was necessary to dissect it and re-suture. An area about 4 cm. was excised. The pathologists reported an ulcer, 3 mm. in diameter, surrounded by a marked sub-epithelial inflammation.

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THE SURGICAL TREATMENT OF GONORRHEAL EPIDIDYMITIS¹

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Urologists are as much at variance in regards to the treatment of gonorrheal complications as they are about the treatment of simple uncomplicated gonorrheal urethritis. Each urologist who lauds his pet drug today may discard it tomorrow for another "would-be specific." In like manner, each one has a pet scheme for treating gonorrheal complications which he believes to give the best results.

Those of us who were interested in the study of gonorrheal epididymitis, during the war seem to be of the opinion that surgical interference in acute gonorrheal epididymitis gives the best results and is termed by some enthusiasts as the ideal treatment. One of the kind lessons impressed upon me during my two years of service, is that nothing was ideal connected with war, not even the "Battles of Paris, Bordeaux, and Nice" in which so many medical officers played a very prominent part. Therefore, I do not then propose to present for your consideration an ideal treatment for the most troublesome complication of gonorrhea, but to review one which is based on pathological findings, common sense, and which has given splendid results in my hands.

In presenting this paper it is my earnest desire to support this form of treatment from my own experience and to especially

¹ Read before the Genito-urinary Section of the Tri-State Medical Society at Spartanburg, February, 1921.

² In preparing this paper I am under many obligations to Drs. Hagner and Cunningham for information given me and from the authors and publishers from which I have taken cuts to make slides, including Gray's Anatomy, Huber and Morton.

emphasize its value in recurrent gonorrheal epididymitis about which I have seen nothing written, per se.

In reviewing the literature on this subject it seems that Pirogoff punctured an epididymis as early as 1852, and Smith in 1864 reported a series of 1000 cases in which he punctured the epididymis with good results. In 1906 Dr. Francis R. Hagner of Washington, D. C., published the technique of epididymotomy and it is largely due to his efforts that the operation

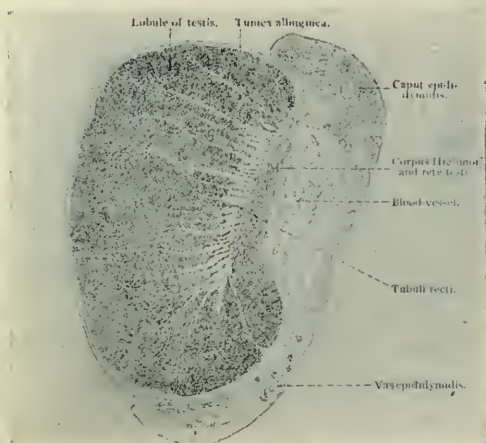


FIG. 1

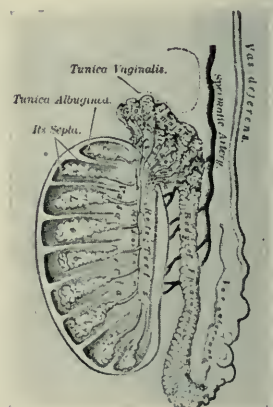


FIG. 2

FIG. 1. LONGITUDINAL SECTION THROUGH HUMAN TESTIS AND EPIDIDYMIS

The light areas between the lobules are the fibrous-tissue septa of the testis; $\times 2$.

FIG. 2. VERTICAL SECTION OF THE TESTICLE, TO SHOW THE ARRANGEMENT OF THE DUCTS

became successful. The surgical treatment of gonorrheal epididymitis, while it is an accepted one, is not properly explained in our popular texts nor do I believe many urologists have studied the histo-pathology upon which this surgical procedure is based. It is with special reference to this part of the subject that I wish to call your attention.

Grossly, this disease passes through two phases: first, an acute inflammatory process with marked swelling in the globus minor,

major and body of epididymis with abscess formation in 60 per cent or more of the cases with the seat of abscess generally in the globus minor (figs. 1 and 2). An accompanying inflammatory hydrocele is the rule and is generally diagnosed clinically as an orchitis which is not substantiated at operation. The time we expect to demonstrate this phase of the pathology is from three to six days after onset. The second stage is from the end of the first week until resolution is complete. In this stage the indurated areas are hard, usually fusiform in shape and as a rule gross pus is *not* easily demonstrated. After the fifth day there is generally agglutination between the visceral and parietal layers of the tunica vaginalis, therefore great care should be taken not to open the tunica albuginea. In this stage we see many cases of acute funiculitis especially if the vas is much involved. When this is encountered the covering of the cord should be opened and drainage instituted.

From a histo-pathological point of view acute gonorrheal epididymitis cannot be considered other than an acute inflammatory process. The pathology produced by the gonococcus in this appendage does not differ grossly from that seen in the Fallopian tube except as the histological structures vary. In the former we have a convoluted tube of very small lumen and in the latter a comparative straight one (figs. 3 and 4). In both appendages the end results is the same, namely, pus formation.

It is difficult to explain why the gonococcus invades one of the ejaculatory ducts and not the other when they are only a few millimeters apart, but we do know that epididymitis is usually unilateral. After an infection of the ejaculatory duct there is generally an infection of the whole lower seminal tract, the infection terminating in the globus minor. In collaboration with Dr. John H. Cunningham of Boston, Dr. Mallory showed in a minute pathological study of resected portions of epididymes that within three days after infection the small ducts are distended with leucocytes and in places there is dissolution of the tissues with abscess formation. In the later stages of the disease, the intertubular connective tissue increases and is infiltrated with lymphocytes. As late as ten days after onset Gram-negative diplococci have been found.

In the chronic recurrent type the pathological picture is quite different and puncture with drainage in these cases gives most excellent results. Macroscopically the covering of the epididymis is very much thickened. Hard and indurated button like masses are found in, but not always limited to the globus minor. This induration is due to the inflammatory changes in



FIG. 3. SECTION THROUGH HUMAN VASA EFFERENTIA

a, Glands; *b*, ciliated epithelium; *c*, glandular structure; *d*, connective tissue

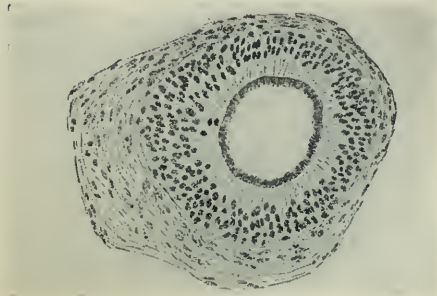


FIG. 4. CROSS-SECTION OF VAS EPIDIDYMIS OF HUMAN TESTIS

the tubular walls and increase in the intertubular connective tissue. The macroscopic demonstration of pus is rare in this type of case.

The Hagner technique is as follows: Under a general anesthetic, the junction of the globus major with the testis is defined,

the scrotum is made taut and a vertical incision about two inches in length is made through the skin down to the tunica vaginalis. If an accompanying inflammatory hydrocele exists, which is the rule, the tunica vaginalis is opened and the hydrocele fluid allowed to escape. In any event the tunica vaginalis is

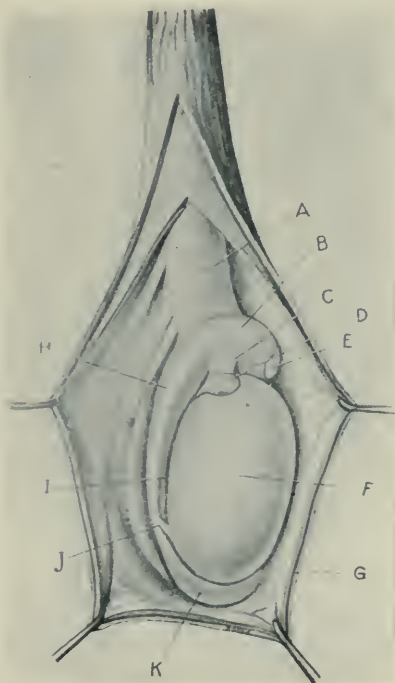


FIG. 5. TESTICLE AND ITS COVERINGS

A, spermatic cord; B, globus major; C, superior ligament of epididymis; D, appendix testis; E, hydatid; F, testis; G, tunica vaginalis; H, epididymis; I, sinus epididymis; J, inferior ligament of epididymis; K, globus minor.

opened just as in a radical hydrocele operation, then the swollen epididymis with the testicle is delivered from the sac. The operator now has the entire epididymis in plain view (fig. 5). As a rule, with close inspection and palpation, the abscess is easily located. Multiple small punctures are made in the covering and penetrating the tissue of the epididymis with the point of a narrow

blade scalpel (preferably a cataract knife) (figs. 6 and 7). If pus exudes, the incision in the covering of the epididymis is enlarged and the abscess opened with a blunt probe. The cavity may be irrigated or sponged out with a 1:1000 corrosive sublimate solution. If a definite abscess is not located then the needle is introduced through the puncture holes and the tissue of the

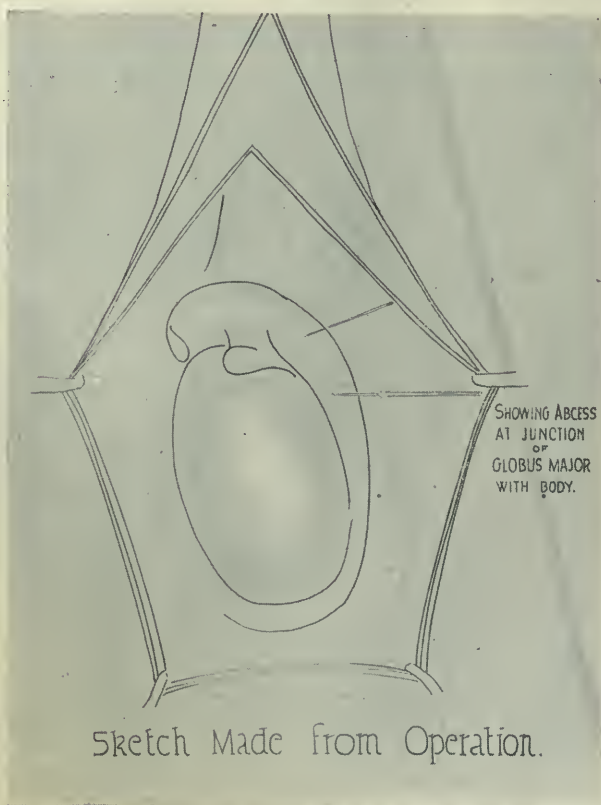


FIG. 6

epididymis needled, for in this way many foci of infection may be located which would otherwise go unnoticed. Drainage is instituted by means of a soft rubber tube or cigarette drain placed alongside the epididymis. Cunningham's method of closing the wound has proven most satisfactory in my hands

which is as follows: two silk worm gut sutures are passed through skin, dartos and tunica vaginalis and tied over a small piece of rubber tubing which is placed on either side of the wound (fig. 8). The testicles are covered with a sterile dressing and supported by means of a suspensory or a shelf made of adhesive plaster.

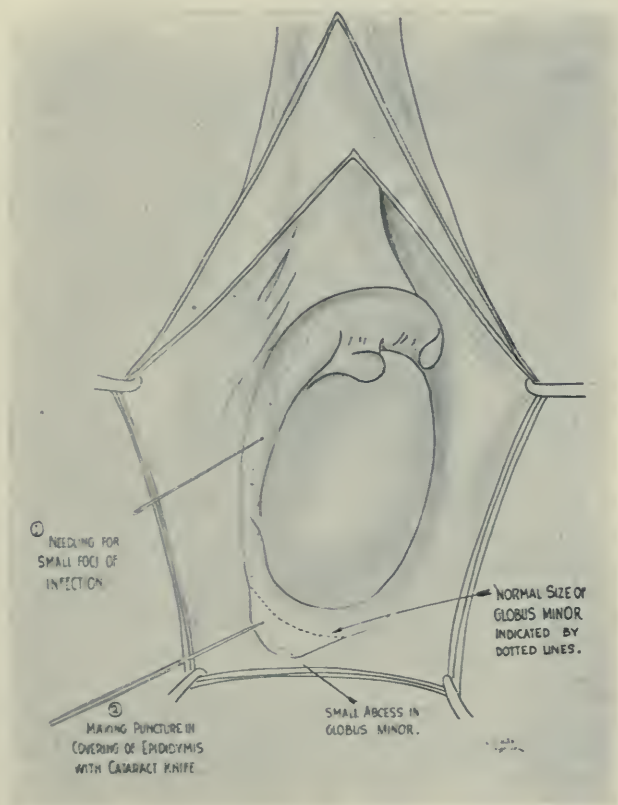


FIG. 7

I wish to emphasize the application of this plan of treatment to the chronically infected epididymis which has a tendency to "flare up's" after dilatation and treatment is resumed on the posterior urethra. In my experience the gonococcus has been very refractory to treatment in this type of case. If the local-

ized foci of infection are punctured and drained, the discharge grows less, the urine becomes clear and the patient is gonococcus free in a comparatively short time.

The above findings are very striking and noticeable in the after treatment of these cases. These are clinical facts which are difficult to understand and which I am at a loss to explain.

It was my privilege to interview Dr. Hagner on this subject a short time ago and it was somewhat of a relief to find that my

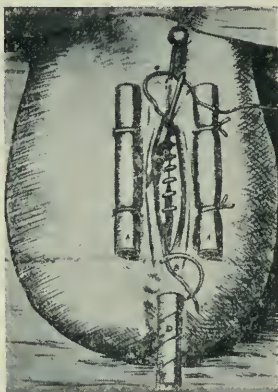


FIG. 8. MANNER OF CLOSING THE SCROTAL WOUND

A-A, two rubber tubes over which are tied the silkworm-gut sutures passing through skin, dartos and tunica vaginalis. B, catgut suture uniting the edges of the tunica vaginalis. C, subcutaneous silkworm-gut suture closing the skin wound. D, drainage tube placed along the outer side of the punctured epididymis.

observations had not been entirely imaginary. Dr. Hagner also gave me this information; that drainage of a chronically inflamed epididymis would *sometimes* clear up a chronic prostatitis which had resisted treatment. He was unable to explain this clinical observation.

This operation is thought by some to be too radical to ever become popular and the "chronic objectors" will set forth two prominent reasons for not operating these cases. First, possible occlusions of the vas epididymidis by trauma or cicatrix following operation in bilateral cases. Second, too great publicity given the disease by hospitalization.

My answer to the first is that the gonococcus has "dug in" and you have to use radical means to get rid of him.

In the three bilateral cases operated on by me I have been unable to make "follow up studies" for spermatozoa. In six bilateral cases operated on by Cunningham he was able to demonstrate the spermatozoa in four after operation two of which have children. Hagner has operated on four cases of bilateral epididymitis—two had spermatozoa and two were sterile following operation. The two having spermatozoa were operated within three days from the onset of the attack.

A proper confidence instilled into patients by frank and fair dealings will minimize the difficulties confronting us about hospitalization.

The advantages of epididymotomy are (a) immediate relief of pain and reduction of temperature with a fall in the leucocyte count; (b) the comparative ease, ridding the tissues of the gonococcus after drainage in chronic cases; (c) the ability to begin treatment in a comparatively short time, with a very much shortened convalescence.

CONCLUSIONS

1. Puncture with drainage of gonorrheal epididymitis is based on a definite pathology which can be demonstrated clinically, macroscopically and microscopically.

2. Histo-pathologic studies tend to support the theory that fewer cases of sterility would exist if drainage was instituted and tension relieved in bilateral cases.

3. In the chronic recurrent type of gonorrheal epididymitis the gonococcus is easily gotten rid of and the patient freed from the symptoms of drainage of the epididymis. (This feature is not easily understood, but is borne out by clinical evidence.)

4. The open operation with drainage is the most efficient and happiest way to terminate the most troublesome complication of gonorrhea.

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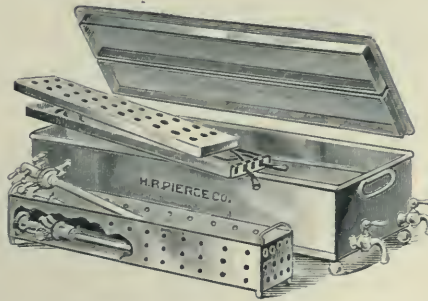
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STERILIZER FOR CYSTOSCOPES

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The need for a compact, efficient, and simple cystoscope sterilizer has been long before us. Though not detracting from the efficiency of the formaldehyde gas sterilizer, the disagreeable odor and the time necessary to obtain sterilization when it is used have made various methods of submergence in germicidal liquids almost the universal custom. With this in view it has been our aim to design a sterilizer for office, hospital, and outside consultation practice that would allow the use of the individual's favorite sterilizing medium, and that would be handy of manipulation and efficient in use. The following design has been made for us by the Harvey R. Pierce Company of Philadelphia.



The illustration conveys the general features and only a few explanations are deemed necessary. The box consists of two water-tight compartments, with a water-seal lid; it is $12\frac{1}{2}$ inches in length, by $6\frac{1}{4}$ in breadth, and 3 inches in height; giving two compartments each $12\frac{1}{2}$ by 3 by 3 inches in size. At one end a faucet enters each compartment for drainage. When in use one compartment is filled with the sterilizing agent. The metal

will withstand oxycyanide of mercury, formaldehyde, carbolic acid, cresol, etc. The second compartment is filled with sterile wash water. The tray, fitting either compartment, is full 12 inches in length, and is walled-up high on sides and ends to avoid the dropping out of instruments. It will easily hold two or three modern cystoscopes unassembled, and thus packed is submerged the desired length of time in the sterilizing solution and then lifted in toto into the other compartment containing sterile wash water, which can be drained by means of the stop-cock at its end, and refilled for repeated washing if desired. A small perforated metal box with lid, fitting into the bottom of the tray, is supplied for ureteral catheters, one end of which has five slots to permit the projection of the proximal ends of the catheters. When packed the ordinary ureteral catheter will make just one and a half turns in the box, so that by submerging the distal end, with the proximal ends in hand, the catheters can be syringed free of air and filled with the antiseptic solution before complete submergence.

For work outside the office or hospital, sterilization and washing can thus be completed, both compartments drained, and the entire sterilizer placed in the ordinary 14-inch professional hand-bag.

PRIMARY CARCINOMA OF THE KIDNEY WITH IMPACTED URETERAL CALCULUS

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CONFUSION IN DIAGNOSIS

In view of the confusion which has so long existed with regard to the differential diagnosis of tumors of the kidney, particularly true malignant disease and hypernephroma, and because of the fact that the question of the origin of these neoplasms is still under dispute, it would seem important that additional cases be reported in an effort to clarify the problem.

Hypernephroma, generally conceded to be the most common renal tumor occurring in the adult, "that tumor whose place is still so indefinite in pathology," is undoubtedly, according to Eisenstadt (1), the most frequent lesion which has been incorrectly classed as carcinoma. From a study of the literature of primary cancer of the kidney, which he found to be replete with reports both of clinical nature and of histologic research, Eisenstadt found from the earliest record at his disposal (the inaugural dissertation of Hullman at Halle, published in 1849) to the time of his own report (1916) a seeming confusion in the histopathologic reports made.

Dunn (2), in an effort to elucidate the origin of hypernephroma, the so-called "Grawitz tumor" of the kidney, reviewed briefly the theories of its origin. Grawitz (3) in 1883, advanced the view that these renal tumors were of suprarenal origin, arising in aberrant "rests" of suprarenal tissue, a theory that was generally accepted for twenty-five years, or until Stoerk (4), from an examination of a large number of kidneys and suprarenals, and

of tumors affecting these organs, concluded that hypernephroma was derived from renal tissue itself, most probably arising from the altered renal epithelium lining papilliferous cysts in the cortex of granular kidneys. Zebe (5) shared Stoerk's conception of the origin of these tumors. Sissons (6), on the other hand, was inclined to accept the view that these renal growths are derived from suprarenal tissue. He pointed out the difference in the distribution of fat in the Grawitz tumor cells on the one hand, and in adenoma of the suprarenal cortex, on the other. Wilson and Willys (7), from embryological studies, considered it unlikely that these tumors were derived from adrenal "rests" in the kidney, since from evidence of development the inclusions of suprarenal tissue under the renal capsule must be rare. These two observers regarded hypernephroma as of renal origin, but derived from rests of nephrogenic tissue, and not from mature renal cells which have undergone metaplasia, as held by Stoerk. Glynn (8) pointed out

that in the comparatively few cases of tumors of the suprarenal cortex which are reported in the literature, the association with abnormality in sexual development is a frequent feature. On the other hand, in cases of Grawitz tumor, which are not very uncommon, such sexual changes are never noted.

From his review of the theories concerning the origin of hypernephroma Dunn concludes that (1) Epithelial abnormalities of the three types described, namely, suprarenal rests, adeno-papillary tissue, and papilliferous cysts, have been found fairly frequently in the kidneys of a series of eighty consecutive cases. The amount of material examined, though insufficient to afford definite statistics, is sufficient to prove that their occurrence is by no means rare. (2) Any of these aberrant epithelial structures might conceivably give rise to malignant tumor formation, but of the three the papilliferous cysts, from their peculiar histological features, suggest themselves as the most probable origin of tumors of the Grawitz type.

Kretschmer and Moody (9) have called attention to the multiplicity of terms used in the diagnosis of tumors of the kidney, especially tumors of the renal pelvis.

RELATIVE FREQUENCY

While hypernephroma, as stated, may be regarded as of frequent occurrence, true malignant neoplasms of the kidney are generally conceded to be relatively rare. Albarran and Imbert (10), for example, in 1903, found only 13 cases of malignant adenoma out of 529 cases of renal tumor. Garceau (11) compiled, from autopsy and operating rooms, a table comprising all tumors affecting the urinary tract at the Massachusetts General Hospital during a period of ten years. Among these he found the following malignant tumors: hypernephromata of large size and of distinctly malignant type, 33; carcinomata, 3; sarcomata, 2; malignant papillary adenomata, 4. He holds that carcinoma of the pure type is a tumor of extreme rarity in the kidney, and he insists, from his personal investigations, that the tumor most commonly found in the kidney is that derived from adrenal "rests," namely, hypernephroma. Eisenstadt refers to one case found by Young from the files of Johns Hopkins Hospital, and three cases found in the ten and a half years preceding 1916 at the Mayo Clinic. Kretschmer and Moody (9), in 1914, found reported only ten cases which resembled the main characteristics of the malignant papillary cystadenoma which they reported, bringing the number up to eleven. Wohl (12), in 1917, added one case, making twelve cases of true malignant disease of the kidney. Kraft (13) reported an unusual case of hydronephroma resulting in medullary carcinoma, with a history of injury and the passage, thirty-seven years before, of nineteen stones, and with malignant degeneration of the hydronephrotic kidney. de Berbe-Lagarde (14) reported a similar case. Hirsch (15) recorded a case of papillary carcinoma of the kidney with metastasis in the brain, which he considered primary. Primrose (16) described a case of squamous-cell carcinoma of the kidney in a horse-shoe kidney with calculous pyonephrosis.

CLINICAL DIAGNOSIS

Braasch (17), studying the clinical records of 83 malignant tumors of the kidney operated on at the Mayo Clinic up to July

1, 1912, classified these tumors according to their histologic structures as hypernephroma (mesothelioma), sarcoma, carcinoma, and embryoma, but pointed out that clinical differentiation, according to this histologic classification, could not be made, as a rule, prior to exploration. From a clinical point of view, therefore, he considered the various forms of tumor together. Complete data of malignant renal tumor (palpable tumor in the region of the kidney, hemorrhagic urine, persistent pain referred to the region of the tumor, and the general symptoms of malignancy) were found in but 32 of the 83 cases studied. Two of the three symptoms were present in 37 cases, and but one in 14 cases. He considers it evident, therefore, that the clinical diagnosis must more often be made with but one or two cardinal symptoms.

The principal problems in differential diagnosis, according to Braasch, are identification of hematuria and upper abdominal tumor. The conditions which most easily may be confused with renal tumor are (1) "essential" and nephritic hematuria, (2) retroperitoneal tumor, (3) bilateral cystic kidney, and (4) closed pyonephrosis. He holds that hematuria, prolonged over a period of several weeks or months, and occurring at long intervals, is suggestive of "essential" or nephritic hematuria, while that which continues but a day or two and reappears at short, irregular intervals, suggests renal tumor. These statements were made before pyelography became a common practice in the differentiation of renal pathology. While a combination of kidney lesion may be present, masking the picture, still a pyelogram renders a diagnosis of renal tumor possible in the vast majority of cases.

Hirsch (15), reporting a case of papillary carcinoma of the kidney, with metastases in the brain, considers that the absence of positive urinary findings need not be taken seriously. In Eisenstadt's case (1) hematuria was present, at intervals, for years previous to operation, not accompanied by pain or other general symptoms. Two years before operation a severe attack of hematuria occurred, accompanied by burning pain in the penis during urination, and dull pain in the right lumbar region, gradually growing worse until operation.

HISTOPATHOLOGIC DIAGNOSIS

The tumor reported by Eisenstadt is considered an atypical proliferation of the secreting cells of the kidney, in many places showing exquisite papillary structure, and as such, in his opinion, could be considered as a carcinoma of the adenomatous type. Papilloma, he holds, as well as the embryonic mixed tumor, or kidney blastoma, otherwise known as adenosarcoma, have repeatedly been described under cancer, adenosarcoma usually as carcinoma of the kidney in childhood. In the case which he reported the minute pathology showed adenomatous or papillary structure, striking in some areas, while in others the cells were arranged in massive compact aggregations. Some of the glomeruli were but slightly changed, some showed changes of hyperplastic character and still others chronic fibrous retrograde changes. The histopathology of this case suggested that these tumors may arise from the glomeruli, instead of from the uriniferous tubules, as some hold.

In Wohl's case of adenocarcinoma (12) he could trace the transition from renal parenchyma into tumor formation. The tissue from the middle third of the tumor showed a great tendency to mimic the tubular structure of the kidney. Wohl believes the contention that primary carcinoma of the kidney does not exist, the argument of those so-believing being based upon the mesodermic origin of the kidney, is untenable, since the renal tubules are lined by epithelium of whatever layer of the blastoderm it comes from, and therefore any tumor arising from it can justly be called adenoma, carcinoma, or adenocarcinoma.

Case report. The case which I wish to report is that of a man, forty-four years of age, married, father of three children, with negative family history. At the age of five he was confined to bed two months with "inflammation of the bowels" (probably appendix). In 1892 he had a sharp attack of left renal colic, but did not pass a calculus. About fifteen years ago he had another attack, following which he noticed that after riding horseback his urine was sometimes claret-colored, but he had no colic or other urinary disturbance. He had no serious illness or urinary symptoms until October, 1918, when he had a severe attack

of influenza. Two weeks after the onset of the influenza he developed profuse hematuria, pain and tenderness in the left upper quadrant and left lumbar region. Later moderate frequency and urgency of urination were noted, and a mass was palpable in the left upper abdomen. He rapidly lost flesh and strength, became decidedly anemic, and when I first saw him, two months after the onset of the symptoms, his condition was as follows: There was profound anemia, the hemoglobin being 33 per cent; the pulse was rapid and of poor force; the temperature varied from subnormal to 102°; tongue coated; appetite poor; emaciation and prostration marked. There was an indefinite mass in the left upper quadrant and lumbar region, which was not hard, was slightly tender and movable. The right kidney could not be felt. The external genitals, prostate and vesicles were negative. The urine was thick with blood and pus. Cystoscopic examination showed a moderately congested bladder, especially the trigone and area about the left ureter, but otherwise negative. Ureteral catheterization showed clear urine, with a moderate nephritis of the right kidney, an obstruction of the left ureter at 25 cm. from the bladder, but a fairly free flow of urine on this side, which showed a large quantity of blood and pus, with poor function (one-fifth that of the right). A roentgenogram revealed a large oval calculus in the left ureter at the point of obstruction to the catheter, 25 cm. from the bladder. Pyelogram showed the renal pelvic outline destroyed.

Cultures showed right urine negative, left, staphylococcus and short bacillus like influenza.

The patient's condition was such that operation was thought inadvisable, and he was placed under close observation. At the end of a week, the hematuria and temperature persisting, loss of strength and anemia progressing, operation was decided upon as a necessity, with the possibility that he would not survive the anesthetic. The hemoglobin was now under 30 per cent, pulse 130, and of poor force.

The preoperative diagnosis was impacted ureteral calculus and pyonephrosis.

Operation, December 21, 1919, under nitrous oxide anesthesia. An oblique lumbar incision exposed a mass of blood clot and pus surrounding the kidney, which had the appearance of being gangrenous. The kidney and clots were lifted out, leaving the kidney capsule. The blood vessels at the hilum were secured with two mattress sutures, the wound was packed with gauze and partially closed with through-and-through sutures. The operation required but a few minutes, but the

patient's condition did not warrant further exploration. The patient rallied from the operation, he improved rather rapidly in his general well-being, the hemoglobin rose to 45 per cent, red blood cells 2,623,000 from 2,212,000, and the right kidney functionated satisfactorily.



FIG. 1. IMPACTED URETERAL CALCULUS. KIDNEY TUMOR

This condition continued for two months, when an induration appeared beneath the surface of the wound, there was a foul discharge from the sinus, and a growth rapidly developed in the flank, which increased in size until, at the time of his death five months later, it extended below the ilium and filled the lumbar region. The appearance on the surface was typically that of carcinoma.

The left kidney, on removal, was of a purplish color, 10 by 6 by 4 cm., flat, smooth on one side, rather ragged on the other; there were no kidney markings and the appearance was that of a softened tumor mass. The surface presented a mottled appearance, as in the photograph. Sections were submitted after operation to Dr. Burton T. Simpson of the New York State Institute for the Study of Malignant Disease, who made the diagnosis of primary carcinoma of the kidney.

I am indebted to Dr. Lawrence W. Strong, head of the pathological department of the Woman's Hospital, for the following careful microscopical study of this specimen, and for the accompanying microphotographs made by him:

The section received shows for the largest part a hemorrhagic and necrotic connective tissue in which the remains of dilated blood vessels were seen. Around and in the neighborhood of some of these vessels are solid alveoli of large epithelial cells with vesicular nuclei which nearly fill the cell bodies. In places the epithelial cells are polyhedral but where the cells are looser they are oval. Many nuclei are gigantic and mitotic. No arrangement in columns is visible save where the cells penetrate a lymph space or spaces in the connective tissue stroma. No stroma can be seen between the cells in the alveoli. The photos and lantern slides we made illustrate the persistence of well nourished carcinoma cells around a large blood vessel. The tissue in the periphery was entirely necrotic.

The second picture shows the variability in size of the cells, the presence of giant cells, the lack of any sign of columnar arrangement or of papillary forms, also hyperchromatosis of the nuclei and irregular mitoses are seen. From the slides submitted one is only able to say that this is consistent with the picture of a medullary carcinoma. Whether it was primarily a medullary carcinoma or not is a matter of conjecture. There is nothing in the sections which suggests a hypernephroma of which the determining characteristics are an arrangement of the cells in columns. The cells of a hypernephroma are character-

istically large, pale, fat—containing cuboidal cells. There may be a papillary or adenomatoid arrangement and the stroma may present



FIG. 2. PRIMARY CARCINOMA OF KIDNEY. GROSS SPECIMEN

appearances suggestive of a spindle-cell sarcoma. A tumor of this sort may also show cells which are distinctly carcinomatous, of very variable size and appearance and with multinucleated giant cells.

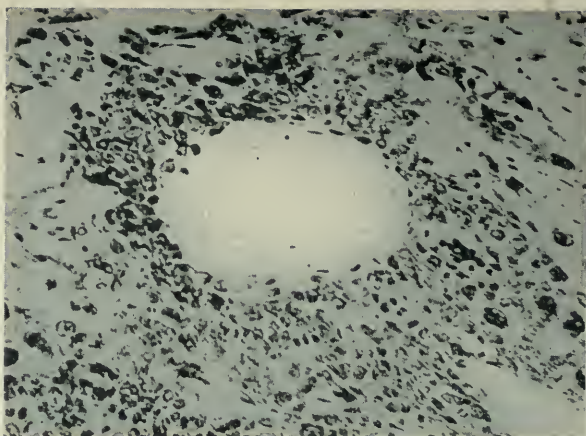


FIG. 3. MICROSCOPIC SECTION OF KIDNEY. BLOOD VESSEL SURROUNDED BY CARCINOMA WITH NECROTIC PERIPHERY

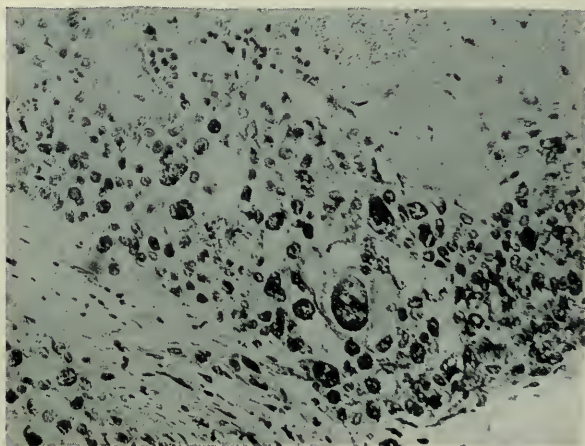


FIG. 4. MICROSCOPIC SECTION OF KIDNEY. GIANT NUCLEI, HYPERCHROMATOSIS AND IRREGULAR MITOSES

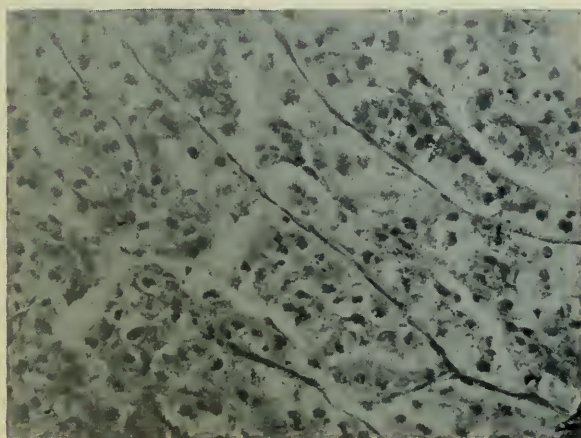


FIG. 5. MICROSCOPIC SECTION OF HYPERNEPHROMA, SHOWING THE CELLS IN COLUMNS. (INSERTED FOR COMPARISON WITH FIGS. 3 AND 4)

Fraser (18) reports a case showing both carcinoma and hypernephroma and it is conceivable that Dr. Bugbee's case is a completely anaplastic hypernephroma, that is that all traces of its original form have been lost by anaplasia. However, there is nothing to justify this assumption; all that the sections present is a diagnosis of medullary carcinoma.

I wish to emphasize the following points in connection with this case:

1. Carcinoma of the kidney is rare, but does occur as a pathological entity, to be differentiated from hypernephroma.
2. The diagnosis cannot be made before operation.
3. The rôle of infection and nephrolithiasis in its etiology is suggestive.

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TRANSACTIONS OF THE NEW ENGLAND BRANCH OF THE AMERICAN UROLOGICAL ASSOCIATION

MEETING HELD AT HARVARD CLUB, BOSTON, MARCH 15, 1921

Meeting called to order by Dr. John W. Keefe, President.

Election of candidates for membership.

PRESENTATION OF SPECIMENS

Dr. J. D. BARNEY: I have a specimen which I would like to show simply for its interest. The patient was a man, thirty-two years old, who was drafted into the army as being in perfect health and went through the war. He was in several engagements and was injured slightly in the knee but had no discomfort at all referable to his urinary tract. I saw him last May, and for about a month he had had a dull pain in the left side and no urinary symptoms whatever—that is the entire history. His urine was hazy, not a dirty urine, but contained pus microscopically and a few blood cells. He had a renal function of 40 per cent. They showed me an X-ray which had been taken, and I thought they were trying to put something over on me. I examined the man, and through the abdomen you could feel a stony hard mass which moved up and down with respiration, and was slightly tender. I thought at first it was a stone in the kidney and then I decided it could not be, but later on it proved to be. I never felt anything like it. I do not think I ever felt a stone in the kidney through the abdominal wall. Later on I took out the kidney the specimen of which I will pass around, together with the X-ray plate. The specimen shows the stone very nicely. You can hold the kidney open and show the large size of the stone and the appearance of the kidney. The kidney was not adherent and it was not a difficult nephrectomy at all. I do not know what the record is, but that is the largest stone I have ever seen in the kidney.

Dr. PHELPS, Worcester: I would like to show a plate and specimen which is of interest. It is a calculus taken from a young man twenty-eight years old, who, two years ago, was shot in the left groin. Recently a piece of material was removed from the back of his right thigh and X-rays of thigh and pelvis (fig. 1) show many particles which appear to be broken shell fragments, but the boy was shot with a rifle and the X-ray shows an absence of the left pubic ramus. His symptoms, when I first saw him, were entirely referable to his bladder, consisting of frequent urination six or seven times at night and every half hour during the day. I cystoscoped him and could see in his bladder a very little

calcified material. But the symptoms were so great that a suprapubic cystotomy was done and this stone (fig. 2) was removed from the bladder. It was fitted into a pocket under the right pubic ramus in such a position that it could not have been seen with the cystoscope.



FIG. 1. SPECIMEN OF KIDNEY REMOVED AT OPERATION, SHOWING ENORMOUS CALCULUS

The assumption is that when the boy was shot in the left groin, the pubic ramus was shattered and particles of it were driven through the bladder, in a downward direction, ruptured the bladder and these particles seen in the X-ray are doubtless calcareous deposit on a piece

of bone as a nucleus. The pathological report of the stone which I removed is "Bone earth (calcium and magnesium phosphates), with a small amount of calcium carbonate and a trace of uric acid." His

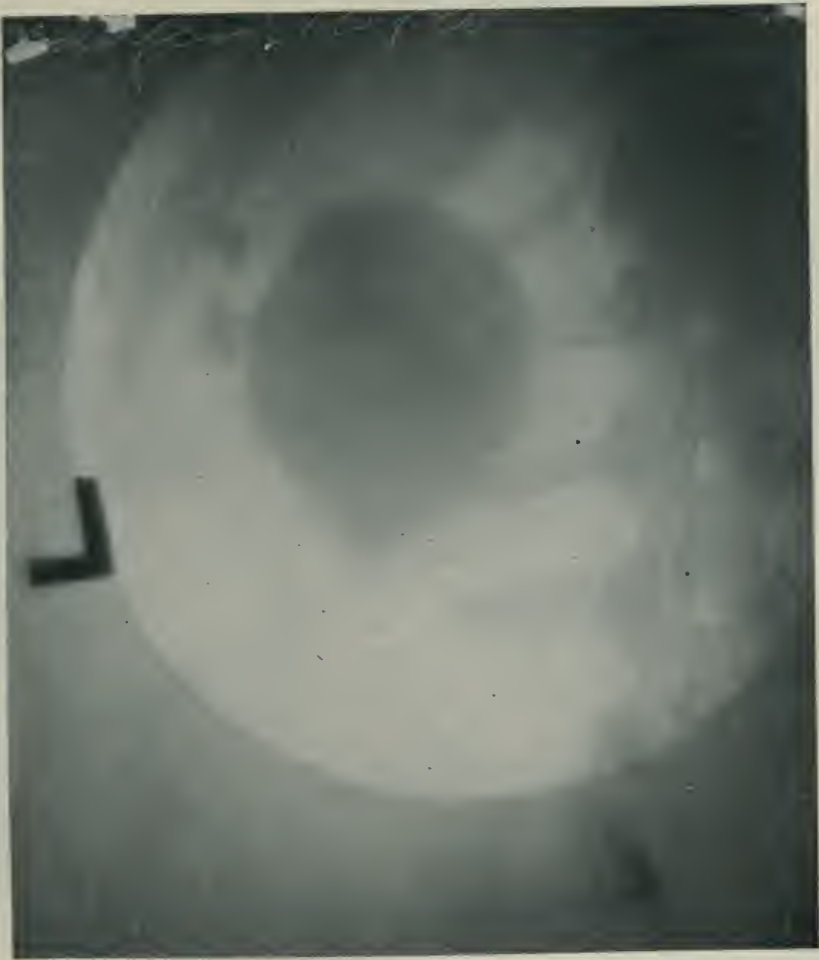


FIG. 2. X-RAY, SHOWING STONES IN LEFT KIDNEY

bladder symptoms are relieved, but he is complaining of a great deal of pain around the right thigh and I suspect the cause to be from some of the other particles shown in the plate which were caused by the extravasation due to rupture of the bladder.

Dr. C. G. MIXTER: We see a great many anomalies in the Children's Hospital, and this case presents a type which I thought might be of interest to the members of this Society. This specimen was from a girl baby, fifteen months old. The family history was negative. The child was brought to the out-patient department of the Children's Hospital and was sent to the gynecological clinic there on account of a profuse vaginal discharge. They sent it down to us in the surgical department, and it was admitted to the house. The mother stated that the child had had straining at stool, had cried with pain and had had this profuse vaginal discharge for a number of months. There had been no blood in the urine and no blood in the stools. The child was very pale, of a yellowish tint, and very sick, and on abdominal palpation there was a resistance in the right side with an indefinite tumor in the right flank. The urine was passed in a clear stream followed by a drachm or two of thick, yellow, foul-smelling pus. We radiographed the bladder, thinking of the possibility of a diverticulum. It was negative for a diverticulum or stone. On catheterizing the bladder a clear urine was obtained. On endoscopic examination with a small speculum and on pressure over the ureter, I saw pus coming from a small orifice on the right side of the urethra external to the sphincter. Pressure on the kidney elicited the same spurt of pus. At operation I found a kidney the upper pole of which was replaced by a good sized abscess cavity, the total size being about three times the normal. The pelvis was greatly enlarged to the size roughly of a hen's egg. The ureter was thickened to about $\frac{5}{8}$ of an inch in diameter. I resected the kidney but did not deem that a ureterectomy was advisable at that time and turned the ureter of the lower end of the wound. The child has since done very well, and it is now ten months since the operation, and there is a slight amount of mucoid discharge from the proximal end of the ureter. There have been one or two times after the operation when there was a backing up in the ureter of pus, and the sinus had to be dilated and washed out. At present no dressing is required. It is one of the relatively rare anomalies of the ureter in which the ureter instead of entering the bladder was implanted in the urethra. It occurs more frequently in girls than in boys. Although the kidney shows very little except the abscess at the upper pole and a dilated and inflamed pelvis, I will pass this around.

Dr. J. W. KEEFE: I would like to report briefly a case where I removed the kidney with a stone which I feel would match the case reported by Dr. Barney. The patient was a woman, forty-seven years of age; she was a weaver by occupation. Eight years ago she was treated for bladder and kidney trouble, at that time passed a stone $\frac{1}{4}$ inch in diameter and one month later passed another small stone. During that time she was unable to work for three months. She has been able to work as weaver most of the time. Three years ago she noticed that occasionally she passed a small amount of blood in her urine. She complained of very severe headaches before menstruation, menses were

regular until one year ago, since then have been occurring at periods of about three months. For the past six months she was confined to bed about one day every month with nausea and vomiting and severe pain over right eye. She had frequent micturition which was usually painless. She passes large quantity of urine and has nocturia two or three times. Six months ago she began passing blood in the urine almost every day. This lasted for three months, from that time to the present, blood in the urine has appeared at intervals, if the patient exerts herself.

Recently she has complained of only very slight pain in the region of the kidney. From time to time there is a large quantity of pus in the urine. Later the urine is quite normal in appearance. December 4 X-ray showed a suspicious shadow in region of right kidney. Was not certain whether it was due to a stone.

December 10, 1920. Operation: Cystoscopy. Under novocaine with preliminary morphine, Kelly cystoscope used. Slightly red about right ureter. Left, normal. Clear urine seen leaving left ureteral orifice. A ureteral catheter was passed but 3 cm. into the right ureter when it met with an obstruction. A ureteral catheter was passed freely into the left ureter.

December 11, 1920. Operation: Nephrectomy. Ether. Right oblique posterior incision made. Kidney delivered into incision—vessels and ureter separately isolated, clamped and ligated and kidney removed. Lower pole of kidney contained two stones like ball and socket, size of hen's egg. Ureter showed very little evidence of disease—upper pole of kidney apparently normal—pelvis of kidney distended and contains stones. Incision closed in layers—rubber tissue drain inserted to be removed in forty-eight hours, also stitch to complete closure when drain removed. Little hemorrhage during operation.

December 13. Rubber tissue drain removed. Stitch tied.

December 20. Stitches removed. Primary union.

The chief points of interest are the size of the stone, the fact that the woman could attend to her work the greater portion of the time and that her general physical condition kept up during that period. (Specimen passed around.)

Dr. J. H. CUNNINGHAM: I wish to present two specimens; one a kidney and one a testicle, which I removed this morning from the same patient. The patient's history and condition present several interesting features.

This gentleman, age fifty-three, has had painful and difficult urination for five years, and a bloody urine for the past two and one-half years. His frequency has been every hour and a half during the day, and eight to ten times at night, during the last few years. For this condition he has had only general treatment of a most miscellaneous sort.

I first saw him in March, 1920, when he was passing bloody urine, with marked frequency. It was possible to palpate the kidney on the

right side, it being about twice normal size. The epididymis on the right was much enlarged, and the prostate and seminal vesicle on the right side suggested tuberculosis. The vas deferens on the right side could be palpated through the inguinal canal, was the size of a lead pencil, and very hard. His general condition was better than fair, his weight being 164 pounds, and he looked to be in good general condition. There were no defects in his general examination other than those referable to the urinary and genital system.

He had been in the volunteer army as a colonel attached to the engineer corps, having been passed physically by the examiners, but not without some dissension on their part. While in the service he received an injury to his leg, and was sent to the Walter Reed hospital, there they discovered that he had a cloudy urine to a palpable right kidney and noted the change in his epididymis. A suspicion was entertained that tuberculosis existed in these organs, and his urine was run through guinea pig tests. The results were negative. Several attempts were made to perform a cystoscopy, which were unsuccessful, because of bleeding.

In March, 1920, I attempted a cystoscopic examination under ether, his bladder capacity being only 2 ounces, but accomplished nothing on account of profuse bleeding.

Repeated smears of the material expressed from the prostate and seminal vesicles by massage showed no tubercle bacilli, but abundance of pus. An X-ray examination of the kidney regions showed an enlarged right kidney, with areas in it which might be interpreted as stones but which at operation were proven to be caseous tubercular areas.

We made three guinea-pig inoculations at different times, and they were all negative.

He consulted almost everybody interested in our subject, and all thought it was tuberculosis. There were five inoculation tests, in all, which were each negative. His general condition did not change much, he lost no weight, but continued to have frequency and cloudy urine during the past year, during which time I saw him occasionally. Operation was refused by him, although urged by everybody who saw him.

This morning I removed a tuberculous right kidney, and the right testicle, which showed extensive tubercular epididymitis as may be seen from the specimen. The vas deferens, upon being divided, exuded about a dram of thick, creamy pus. The cut end of the vas was left on the skin surface to drain.

The most interesting features of this case to me are that a man can go on with such extensive tuberculosis of the kidney, bladder, and genitals, for over five years, without changing his general condition. This patient is a mayor of a nearby city, and his duties have been arduous. He has lost no weight and his general condition had been good at all times.

Another interesting point is the fact that it has been impossible by repeated examinations of the urine and expressed material from the

diseased genital organs, to find the tubercle bacillus. We are convinced that occasionally a kidney becomes occluded when diseased by tuberculosis, but in this instance there is a tubercular bladder, and of course the genitals have an avenue of escape for their products so that it is surprising that a perfect diagnosis could not be made by the repeated guinea-pig inoculation tests.

In other words, in this instance the usual means of diagnosis for the indications of operations were not to be had.

Another point of interest, which is demonstrated in this case, is the fact that we have the co-existence of tuberculosis of the kidney and genital tract conditions which I believe are quite commonly associated, which point is one which has been argued at length at previous meetings of this Association.

THE VARYING TYPES OF PROSTATIC OBSTRUCTION¹

ALEXANDER RANDALL

Philadelphia

I have accepted the privilege of addressing you this evening on "The Varying Types of Prostatic Obstruction," firstly because it is ever a live subject in our speciality and secondly because the material at hand probably presents the subject from a new point of view. Possibly I will be able to correct some old fallacies, possibly to start some new thoughts and ideas relative to your individual experiences that will lead us to draw further valuable surgical lessons for the future.

It is not my purpose this evening to read to you a lengthy essay on the subject of prostatic obstruction, but rather in a way different from the accustomed mode, interest you in my subject by lantern slides of actual prostatic conditions as found in a series of over eight hundred autopsies that I have been recording during the past seven years.

Yet I cannot refrain from telling you how I hesitate to approach this subject and its varying phases, whose history is probably more intimate to many of you in my audience, who have lived through the years of controversy, than to me, for on its pages the surgeons of Boston have writ in large, bold type, some of the most interesting chapters.

It troubles us but little tonight, whether in searching for etiologic factors we follow the teachings of Ciechanowski and believe in an ancient chronic inflammation as the underlying cause, or with Guyon and his school look upon a bladder, impotent from arterio-sclerotic changes as the important factor. Nor whether we enlist with Virchow and Cohnheim and believe it neoplastic, or agree with Hallé and Motz that it represents an

¹ Read at a meeting of the New England Branch of the American Urological Association, Boston, March 15, 1921.

hyperplasia secondary to oft-repeated and prolonged congestion. I would, but for a moment, draw your attention to the increasing acceptance of the theory of inter-glandular hormone activity between the testis and the prostate and then for the etiology leave you with the conclusion of Richardson that this "change in the prostate appears to be as common as grey hairs." Or better, perhaps, with the more classic quotation from Sir Benjamin Brodie,

When the hair becomes grey and thin, when atheromatous deposits invade the arterial walls, when there is formed a white zone about the cornea, at the same time ordinarily, I dare say invariably, the prostate increases in volume.

Moreover, and perhaps more strangely still, I will omit an exposition of the microscopic pathology of prostatic changes. There is no need to traverse once more all this old-beaten ground. We care not for the present to agree with Albarran, Hallé, Rindfleisch or Billroth that the primary change is a fibro-muscular one, for fear of offending the theories of Alexander, Gouley, Moullin and Geraghty of the primary activity being in the epithelium of the acini. The thought of today has not yet crystallized into a theory or fact sufficiently pure to gain general acceptance.

I do believe, that speaking broadly, but three different types of changes are met with in this gland and in their purity I may call them (1) a glandular hyperplasia, (2) a fibrosis, and (3) a neoplasm.

These studies and conclusions have been derived from somewhat different methods of investigation than the usual. The greater part of our knowledge has been acquired by intensive study of clinical material both before operation, and from specimens removed at the operating table. Ciechanowski and Albarran alone sought the autopsy table for a long series of specimens and based their valuable conclusions on the gross and microscopic study of the material there found. I likewise have tried in my work to reverse the usual procedure, possibly perforce for lack of greater material, and have examined the pros-

tate and bladder and their adnexa in eight hundred males as they came to autopsy at the Philadelphia General Hospital. All ages have been examined, though of course the majority in their elder years, and this material has been mounted, drawn and photographed. The question immediately springs into your mind, How did you know that these patients suffered from urinary obstruction during life? Wade says,

How often during the post-mortem examination of patients who have died of various diseases in the medical wards of the hospital, there can frequently be observed, in male subjects over the age of fifty years, indications of a mild degree of chronic prostatic disease with associated damage to the urinary tract above. It is virtually always found that no complaint has been made of this by the patient. It is usually unsuspected, and has virtually never received treatment. In these cases, however, the ureters and renal pelves are dilated to a moderate extent and there is present a recent interstitial nephritis throughout both kidneys and the renal parenchyma shows indications of pressure atrophy through its substance. When the pathology of these cases is reviewed by one with a surgical mind, it is impossible to avoid the conclusion that the renal destruction, as a result of the partial retention of urine from the prostatic disease, has contributed to a certain extent to lowering the patient's power of resistance to a general infection, or has poisoned the heart muscle by the retained products of metabolism which should be normally excreted by the healthy kidney.

Added to these renal changes the outspoken pathology that exists in the trabeculated bladder wall, the dilated ureters, the deep bas-fond formation, perhaps a diverticulum or two, and your circumstantial evidence of vesical obstruction is so complete as to convince the general surgeon or internist, let alone the trained urologist. In the majority of cases these stigmata have been so self-evident as to demand explanation rather than inquiry, and as an actual matter of fact these, and only these, are oftentimes the signs and symptoms which we use cystoscopically to diagnose the obstructive nature of prostatic lesions. These patients succumb to other lethal affections, and their clinical and anatomico-pathological diagnoses rarely take into account the part played by the urinary obstruction. These are

the evidences that I have taken as indicative that the pathologic changes found at the vesical orifice did actually cause urinary obstruction during life. The part played by this obstruction in the individual's death has frequently presented a beautiful sequence of clear deductive reasoning where it has been possible to see it both from the experience of the postmortem examinations and the training from clinical observation. What I mean to convey is this: That clinically we frequently see an old prostatic verging on uremia, with weakened myocardium, and chronic interstitial nephritis pick up under treatment, withstand operation, and live on to years of health and comfort, oftentimes better and stronger than for years before. Contrariwise in this study it has been possible to view the opposite where the resistance (unfortunately sometimes the diagnosis) has been lacking and we see at the autopsy table the whole story unfolded of how a primary urinary obstruction has been the impelling force that started the downhill trend that ended in catastrophe. Moreover it was easy by going back to the clinical histories of these autopsy cases to find in many instances complaints that had been considered trivial or unimportant, or symptoms that were not followed out to their ultimate conclusion. The continual stimulation to seek further has been the interest aroused by these mistaken diagnoses, and the interpretation of symptoms as revealed by the anatomical findings and the light thrown by so vast a material into the practically unlimited variation that obstructive growth can assume.

Here let me digress a moment to point out to you how much more fond is the average pathologist, when doing an autopsy, of monotonously measuring the mitral valve leaflet counting the number of ribs to the dome of the diaphragm, pointing out the Malpighian tufts in the spleen, or painstakingly describing the character of the parietal adipose tissue than in the exposition of the male pelvic pathology. To the average pathologist of today the normal and pathological characteristics of the prostate, seminal vesicles, and testicles are inviolable secrets.

And now to the material at hand. I have divided it into four groups that I might demonstrate more clearly the varying

pathology: (1) The usual generalized prostatic hypertrophies. (2) The isolated median hypertrophies. (3) The obstructing median bar cases. (4) The malignant growths.

Under the first group of generalized hypertrophies the interest is immediately aroused by the variety of types that this may assume. The earliest evidence of lateral lobe enlargement is a beginning protrusion from one or both sides into the urethral lumen. This is often very decided before the lateral lobes themselves appear enlarged and apparently may be well marked before encapsulation by the pressure of hypertrophy is established. This means that enucleation in such cases would entail more difficulty and not allow of as clean a cavity after the adenectomy as in a further advanced case. This lateral protrusion is easily visible cystoscopically and the necessity for operation in such cases should be judged more upon the amount of residual urine than on the fact alone that hypertrophy is present. There are other cases in which a relatively equal degree of hypertrophy exists, but in which it has its origin deeper in the lateral lobes and causes less intraurethral growth, more extra-urethral pressure and earlier encapsulation.

From these early manifestations the grades of hypertrophic growth extend upward to almost an indefinite size. The usual growth remains fairly symmetrical with equal hypertrophy in either lateral lobe, though it is in nowise extraordinary to find one lateral lobe forming a definite intra-vesical projection with but slight tendency toward enlargement of similar character in the opposite lobe. In the enormous hypertrophies one sees varying degrees of dilatation of the internal sphincter, and upon this depends the extent and character of the intra-vesical herniation. When the sphincter and trigonal muscle remain strong the hypertrophy raises the entire floor of the bladder without distortion of the viscus or its orifice and may attain enormous size without apparently effecting the bladder's symmetry. In such a case, the posterior urethra is greatly lengthened, the growth seems much more strongly encapsulated and keeps the contour of an inverted truncated cone. Obstruction in these cases is due to the lifting of the entire vesical orifice plus the

compression on the walls of the urethra by the enlarged lateral lobes. When, as is more frequently the case, the sphincter is dilated and the hypertrophy herniates through it into the bladder cavity, it obstructs and distorts the vesical orifice, creates a deep trigonal and post-trigonal pouch, becomes more rounded in shape, and less definitely encapsulated, though more readily enucleated. The mechanical obstruction to urination here is one of hindered sphincteric function, dam-like distortion of the vesical orifice and the creation of a dependent bas fond with its subsequent weakened bladder wall.

There have been a number, twenty-nine in all, of plain lateral lobe hypertrophies unassociated with the development of true median lobe enlargement, though let it be constantly borne in mind that in these cases the posterior prostatic commissure usually shares in the hypertrophic process forming a sub-cervical thickening of definite obstructive character.

Tri-lobular hypertrophy is of about equal frequency, there being recorded twenty-two such specimens where the median and both lateral lobes show a definite enlargement. In this series of autopsies numerous excellent examples of such growths have been observed but I will omit a further description as they represent but a combined effect of the fore-mentioned type with the more interesting solitary median enlargements that I wish to give a special exposition of next.

Tandler and Zuckerkandl, Albarran and Motz, Wade and especially Lowsley have not only conclusively shown the frequency of median lobe hypertrophy but have demonstrated that the origin of this type of obstruction arises from the sub-cervical glands lying under the mucous membrane just distal to the vesical lip. That you may appreciate my desire to dwell at length on median lobe hypertrophy let me quote from a recent authority who disagrees with the foregoing views to illustrate how clinical experience, no matter how vast, may betray the truth. Freyer in the fifth edition of his "Enlargement of the Prostate" (1920) reports his conclusions based upon an experience of one thousand six hundred and twenty-five prostatectomies. On page 2 he says,

A third, or "median" lobe, was described by Sir Everard Home in the early part of the last century as existing in the normal prostate, and this description has been almost universally accepted as correct, in spite of the fact that Sir Henry Thompson with great skill combated the existence of this lobe. Practical experience has convinced me that Sir Henry Thompson was correct in his views, and that the so-called "middle" lobe is merely a pathological product, derived from one or both lateral lobes, and that it is non-existent in the normal prostate.

I do not need, before this audience, to quote Lowsley's work on the embryology, proving the presence of sub-cervical glandular tissue in 98 per cent of all male urethras, which when hypertrophied, forms the true median lobe obstructions. It is

TABLE 1
800 autopsies; 157 prostatic abnormalities

	NUMBER	PER CENT
Lateral lobe hypertrophies alone.....	29	18.4
Median lobe hypertrophies alone (subcervical)	42	26.7
General trilobular hypertrophy	22	14.0
Anterior lobe.....	3	1.9
Carcinoma	8	5.0
Sarcoma	1	0.6
Median bar—fibrous	8	5.0
Median bar—glandular	13	8.2
Median bar—not classified	18	11.4
Median bar—small and non-obstructive	14	8.9
Total	157	

beyond imagination that Freyer's "So-called 'median' lobes," if truly but pathological outgrowths of one lateral lobe should consistently assume such uniform and symmetrical hypertrophies as I will show you, or that the hypertrophy should gain such size as some of my specimens and be devoid of visible lateral lobe overgrowth. This median lobe hypertrophy has been so frequent an observation that I am almost ready to agree with Tandler and Zuckerkandl, that these tubules are never free of hypertrophy when the prostate enlarges, though feeling that in some instances the microscope would be necessary to confirm the

judgment. I have seen 42 cases of solitary median lobe hypertrophy in this series of 800 autopsies and in 22 other instances a median hypertrophy has been associated with lateral lobe enlargement, (true tri-lobular hypertrophy), making a total of 64 such median lobe cases. I will show you solitary median lobes, no larger than a dried pea, yet so obstructive that massive trabeculation of the bladder musculature has developed, while in other instances hydronephrosis was present. I have found it in men from thirty-six to eighty-five years of age, and have specimens where it has attained the size of the distal phalanx of your thumb, without lateral lobe involvement. I have cut sections in the mid-line to show its superficial, sub-mucous position, and have dissected or enucleated it to prove its separate encapsulation and absolute freedom from lateral lobe attachment and am convinced beyond peradventure that it is the most frequent, the most obstructive, and oftentimes the solitary form of hypertrophy macroscopically, and that is clinically, present.

This type of true median lobe is an hypertrophy in the sub-cervical glands of Albarran, and is not at all to be confused with the deeper gland tissue in the posterior prostatic commissure, which he called the pre-spermatie group of glands, and which he, in his work with Motz, claimed were almost uniformly hypertrophied, while at the same time stating not to have encountered a single instance, in his 107 specimens, of solitary sub-cervical hypertrophy. I was quite surprised to find this statement in their article, for in my series this type of solitary hypertrophy has been the most frequent to be found, and I will demonstrate to you the distinct differences between these two types of hypertrophy and be able to show you specimens that are, I believe, sufficiently convincing wherein the sub-cervical glands alone are hypertrophied and are also definitely obstructive. My object is to prove that even these cases, though clinically undiagnosed as in need of operative interference, were nevertheless suffering from definite urinary obstruction and that the picture is not one only of a casual post-mortem find.

There should be a distinct differentiation made between these two types of median obstruction; anatomically different and

ofttimes clinically different, they are distinctly different, at the operating table, and upon an appreciation of this fact with the different handling of the two types, the perfection and permanence of the operative result will depend. We have all seen the patent urinary fistula after either the supra-pubic or the perineal prostatectomy, and we are prone to explain it by supposing tabs of redundant mucous membrane acting as valves. Possibly at times true, but candidly I believe that in the vast majority of cases easily enucleated lateral lobes have been removed, while deeper and more truly obstructive hypertrophic prostatic tissue has been allowed to remain. It would surprise you to see how deeply under the trigonal apex these growths can extend. Where else could they be more perfectly placed to hamper the action of the sphincter and the detrusor muscle?

This leads me directly to the subject of median bars, on which I wish to dwell but briefly and to recall to you anatomical points of operative importance to which I have elsewhere drawn attention. Firstly, the so-called median bar is purely a clinical term, used to designate an obstruction to the bladder that cannot be accounted for by lateral or middle lobe hypertrophy. Secondly, such obstruction may be due to either of two distinctly different pathologic changes. Thirdly, the choice of operation should depend upon a knowledge of the type of obstruction existent. These types of pathologic changes, are, first, a true fibrosis, and in this distinct pathologic difference from an hypertrophy it would perhaps be better to restrict the term median bar to it alone, except that the second pathologic change, a localized hypertrophy, gives a clinical picture identical with the first. With a nice appreciation of the difference between these two pathologic processes, it is not beyond ones power to differentiate cystoscopically between the fibrotic and the hypertrophic bar formations and with this distinction and its recognition to so vary ones operative procedure as to suit the problem at hand. Nothing is more disgusting than to find an otherwise broad-minded surgeon completely wedded to the narrow rut of one operation and shoving his patients into his operative planing-mill, all to come out cut to the same thickness, mould and groove,

the fortunate ones worthy of inspection and a finished product; the misfits, scarred, splintered, showing their knots, and possibly being prepared for someone else's pet operation.

And by what different operative procedures, you may ask, are these cases to be handled? I feel the true fibrotic bar should be destroyed; the elevated vesical lip, the sclerosed sphincter, the narrowed orifice, the tortuous urethra, should be rectified. This may be accomplished in one of three ways, fulguration, punch operation, or open dissection. I might add a fourth way, that by cautery destruction at an open operation. The second type due to hypertrophy of gland tissue calls for closer study and nicer operative choice. When the hypertrophy is in the sub-cervical glands alone, is discreet, partially pedunculated, superficial, and not too large, the punch operation should remove all; but when this hypertrophy is in the posterior prostatic commissure, in what Albarran terms the pre-spermatic glands, is deep seated, rounded, and broad-based, then the open operation is essential, complete enucleation or cautery destruction being called for.

These are the facts that makes me state that the median bar is firstly but a clinical term; with, secondly, a varying pathologic process causing its formation; and thirdly, with a diversity of operative procedures individually applicable only when the underlying changes are appreciated.

The frequency with which cancer has been present in this series is not a true indication of its occurrence in operative cases, for the material has not been systematically sectioned for microscopic study. Its occurrence is low, only 4 per cent in the grossly pathologic specimens and they show but few changes that are not already well understood. The encroachment on the urethra, so generally appreciated, on attempted instrumentation, is easily demonstrated in the dense, firm, adherent, inelastic lateral lobes, with as a rule a total absence of increased urethral lumen so characteristic of the benign hypertrophies. One outstanding feature found in three specimens is a malignant infiltration of the bladder wall as a result of a primary carcinoma of the prostate. It has been generally thought and taught that pros-

tatic cancer remains for a long period restricted to the limits of the gland's capsule and that ultimately death comes from distant metastasis. This has been the case in the majority of specimens, and several times the autopsy protocol has been corrected to read primary carcinoma of the prostate with secondary metastasis to other organs at first thought the primary seat. But in the three specimens above referred to the malignant growth has spread both superficially along the urethra to the trigone and in one case apparently without mucous membrane involvement directly into the bladder musculature. Evidences of great bladder obstruction are generally present with marked trabeculation of the musculature, and where the growth has involved the mucous membrane a peculiar mosaic mottling of the bladder floor, due to the infiltration of nodular malignant proliferation, has been its most outstanding diagnostic characteristic. As regards the metastasis of prostatic carcinoma it may be of interest to note that in the seven cases where such had occurred the pelvic and retro-peritoneal glands were affected in three; the pancreas, liver, and lung in two; while the spleen, the parietal and visceral peritoneum, the ribs, vertebra and iliac bone in but one case only, and all these bone metastases occurred in one of the eight cases of malignancy. One case of prostatic sarcoma has been encountered.

Dr. A. L. CHUTE: I think we are to be congratulated on hearing such a fine paper. It is tremendously enlightening and it has helped me to visualize the various types of obstruction. I do not think there is much in the way of discussion to be added. The subject has been gone over wonderfully well and I feel personally indebted to Dr. Randall for coming and giving us this treat.

Dr. CUNNINGHAM: I do not see how anybody is going to adequately express his appreciation of Dr. Randall's paper. Such a study seems to me the keynote in the intelligent understanding of this subject. One can recollect Dr. Watson's monograph in 1888, which was the foundation of the modern conception of the different forms of hypertrophy of the prostate, and Dr. Randall tonight has amplified what Dr. Watson pointed out in 1888, which is indeed gratifying, inasmuch as there is a tendency to lose perspective in regard to this subject, because of the multiplicity of details connected with it.

There are so many things that can be dwelt upon in Dr. Randall's

paper that one hesitates to start, but he has spoken of two things which I feel have most important practical bearing, and which bear accentuation; one is the great fallacy which is growing into prostatic surgery of subjecting all patients, no matter what type of obstruction exists, to one operation. I think that if any one thing that Dr. Randall has shown us tonight is more impressive, it is that we have a tremendous variation in the type of hypertrophy producing obstruction; and with his physical difference it is not proper that we subject our patients to one type of operation. I think he has brought this out very clearly, but I cannot refrain from accentuating it.

The other point which impresses me, and which I believe is little appreciated, is the importance of the extension of the prostatic hypertrophy underneath the trigone in certain instances. I think certain specimens, which he has showed, illustrate this clearly; and I believe that failures to relieve obstruction by whatever operative method, is due to not recognizing, in some instances, this extension beneath the trigone.

Failures to get relief of obstruction by operation and persistent sinuses following operation, are more frequently due to the failure to remove this prostatic tissue beneath the bladder mucuous membrane than to anything else.

Dr. TOWNSEND: It has occurred to me from hearing Dr. Randall's description which he has given us of the pathology of prostatic obstruction to ask him whether or not we are to remove portions of the gland which are not obstructive as well as those which we determine are obstructive. I would like to hear from Dr. Randall on the question whether he does a prostatotomy or a prostatectomy.

Dr. R. F. O'NEILL: I am sure there is nothing I can add except my very great appreciation of Dr. Randall's series of specimens. I agree with Dr. Cunningham that it shows us the fallacy of trying to deal with all types in the same way. I can see this from some of my own cases, which were not all they might have been from the failure possibly to remove some of the lobules which were left. I think also that he points out the usefulness of certain types of the lesser prostatic operations such as the median bar excision and various other methods of dealing with the horse collar and not the mass hypertrophies. I think there are numerous cases in which a careful cystoscopic study would enable us to deal with that type of obstruction more than we do.

Dr. J. D. BARNEY: I have nothing to add except my sincere thanks for and my appreciation of the splendid work that Dr. Randall has done. I agree thoroughly with Dr. Cunningham and Dr. O'Neill who have said that one type of operation is certainly not what we should always have in mind. I think that Dr. Randall has pointed out more clearly than it has been done before that there are some types of prostate which can be removed better by the perineal route than by the

suprapubic, and I have had many experiences where I could have got them out better by the perineal route doing a bimanual operation where one could not get all the lobules out which lie so deep in the prostatic urethra. If the lobules can't be reached from above some of them can be reached from below; and if one can do a combined operation, one can succeed where he otherwise would fail.

Dr. RANDALL (closing): I have looked for a great deal of discussion and pointers. The work has been interesting and instructive. Unfortunately it was undertaken and started without any great idea of what it was going to bring forth. And this invitation was the first incentive I have had to begin to tabulate the material. I did it in the beginning, looking for median bars. I thought in the beginning I had a good idea of what a median bar was, and fortunately some of the first specimens I had were of the median bar type; then I found other types of obstruction, some of which varied immensely, and I found other forms of hypertrophy; but it is interesting to see the relative importance of the changes which take place.

In reply to Dr. Townsend's question with regard to removing all the prostate—I think it ought to be done. There are certain parts which are the more obstructive parts, but I think we have all experienced—I have in the case of a man from Alabama in whom at the second operation I removed large hypertrophied lobes—that in a large number of cases a supposedly complete hypertrophy has been removed only to have other glandular tissue left behind become obstructive. So I think that all hypertrophied tissue should be removed.

Let me say that it is not essentially true, but nevertheless oft-times obvious enough to be worthy of mention, that a great many surgeons look upon hypertrophy of the prostate as a sort of classical entity to be found routinely of a fairly uniform type of growth, and its removal to be accomplished by finding a line of cleavage and enucleating all that can be obtained by blind finger dissection. My own experience is so at variance with this concept that I wish in ending to focus your attention on this one fact that the variety of topography that the prostate may assume in hypertrophy is unending, and if one thing alone will sufficiently apologize to you for my choosing such a subject as prostatic hypertrophy for my address this evening it will lie in bringing to your close attention the realization of some of these varying forms of enlargement, that your surgery may be guided into an effort to enucleate hypertrophic tissue wisely, surgically and completely.



FIG. 1. No. 4177. Blockley. Age fifty-six. Clinical diagnosis: Chronic interstitial nephritis. Anatomical diagnosis: Ditto, chronic adhesive peritonitis, and pleurisy. Specimen of early hypertrophy of prostate with median hyperplasia and a glandular bar. Note marked intra-urethral proliferation.

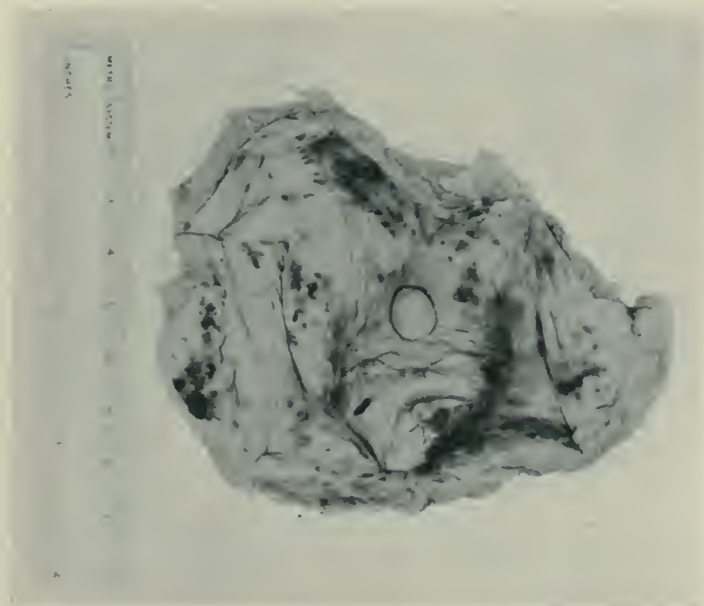


FIG. 2. No. 5448. Blockley. Age seventy-eight. Clinical diagnosis: Cerebral apoplexy, motor aphasia, chronic nephritis. Anatomical diagnosis: Broncho-pneumonia, cardiac hypertrophy, mitral and aortic stenosis, chronic interstitial and parenchymatous nephritis. Specimen a most unusually beautiful example of the obstructive nature of a small median lobe hypertrophy, showing perfect ball-valve position. Suprapubic aspect.



FIG. 3. No. 4504. Blockley. Age seventy-seven. Clinical diagnosis: Em-
pyema. Anatomical diagnosis: Ditto, sub-acute peritonitis, chronic interstitial
nephritis. Specimen exhibits a small hypertrophy of Albarran's subcervical
glands. It has been incised to show definite localization and encapsulation of
this type of hypertrophy and its freedom from the lateral lobes and its position
outside the capsule of the posterior commissure.

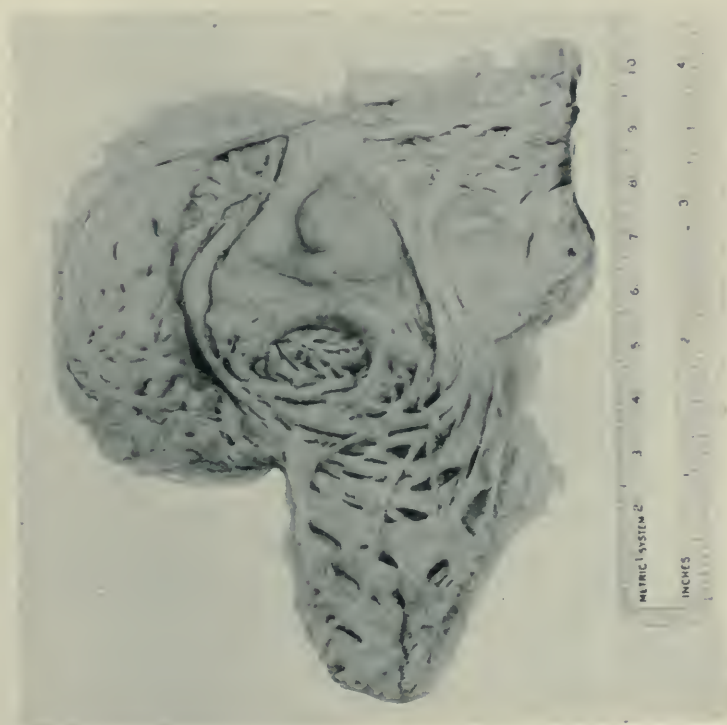


FIG. 4. No. 5679. Blockley. Age eighty-one. Clinical diagnosis: Chronic myocarditis, arterio-sclerosis, fracture of femur. Anatomical diagnosis: Ditto. Specimen of bilateral benign hypertrophy, mounted to show supra-pubic view. Note the greater advancement of the right lobe through sphincter causing crescentic orifice with cleftings at upper and lower right segment.



FIG. 5. No. 254. Methodist. Age ? Clinical diagnosis: Uremia and hypertrophy of prostate. Anatomical diagnosis: Ditto. Specimen shows prominent intravesical projection of right lateral lobe with a slight median lobe. Note urethral bulging; probably a rotated prostate. Hemorrhagic cystitis and ureteritis with left hydro-ureter.

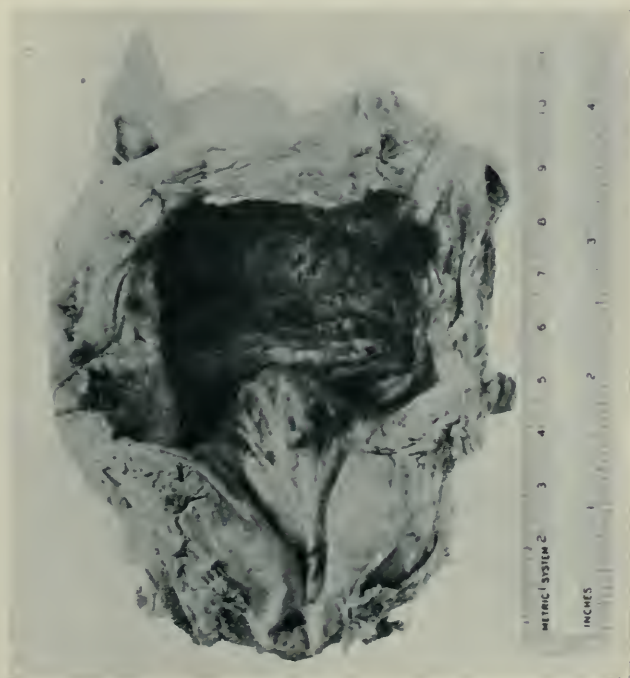


FIG. 6. No. 5517. Blockley. Age seventy-eight. Clinical diagnosis: Chronic myocarditis, hypertrophied prostate, supra-pubic cystotomy. Anatomical diagnosis: Ditto, chronic endocarditis, chronic interstitial nephritis. Specimen a beautiful example of advanced median lobe hypertrophy with perfectly symmetrical projection into the bladder cavity. There is moderate lateral lobe hypertrophy also.



FIG. 7. No. 4186. Blockley. Age seventy-six. Clinical diagnosis: Lobar pneumonia, hypertrophied prostate, hydrocele. Anatomical diagnosis: Ditto, chronic interstitial nephritis. Specimen a large hypertrophy of the prostate with hypertrophied and trabeculated bladder walls. Note actual widening of urethral lumen and natural cleavage line used in enucleation of the gland at operation.



FIG. 8. No. 5656. Blockley. Age eighty-four. Clinical diagnosis: Senile dementia, chronic myocarditis, chronic nephritis. Anatomical diagnosis: Terminal pneumonia, chronic myo- and endocarditis, senile nephritis, and hydro-ureters. Specimen shows typical heavy, thick, firm, enlargement due to cancer. Note difference of orifice, lack of median hypertrophy, and increased vascularity. Also no bas fond formation.



FIG. 9. No. 4276. Blockley. Age eighty. Clinical diagnosis: Chronic interstitial nephritis. Anatomical diagnosis: Gouty kidneys, hydronephrosis, and double hydro-ureters. Specimen shows an enormously hypertrophied and trabeculated bladder wall and an isolated enlargement of the median lobe. The thickened bladder wall on right on section show carcinoma as do sections from the prostate.

TREATMENT OF GONORRHEA AND ITS COMPLICATIONS WITH VACCINES

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From some of the many reports regarding the use of vaccines in the treatment of gonorrhea and its complications, it would seem that the chief benefits were obtained in systemic conditions and not at the time of purely localized symptoms when the infection is restricted to the surface of the anterior urethra. As early as 1909, Schindler (1) considered that the indications for vaccine therapy were limited to cases of epididymitis, chronic prostatitis, urethritis and gonorrhea of the adnexa. In epididymitis he used vaccine only in severe cases and remarks that after this treatment indurated areas remain which require other procedures, such as puncture, incision, fomentation, etc. He says vaccine has no gonococidal action, for the gonococci multiply in cases of acute gonorrhea treated by vaccine, and he has seen epididymitis and salpingitis develop in spite of vaccine injections. Friedlaender and Reiter (2) found that vaccine treatment gives good results in acute and sub-acute gonorrheal epididymitis and in follicular prostatitis, but not in acute or sub-acute gonorrheal arthritis. The vaccines used were not of the mixed or autogenous variety and contained five million gonococci per cubic centimeter. Small doses are recommended.

J. O. Hirschfelder (3) claims a fair degree of success with digestive bacterial extracts. The extract was prepared as follows: suspension of the gonococcus was heated to 38°C. (100.4°F.) and to it an equal quantity of 0.2 per cent solution of pancreatin in 2 per cent sodium bicarbonate at 38°C. was added, kept at temperature for fifteen minutes and then acidulated with hydrochloric acid. The mixture was then filtered through a Pasteur filter and was ready for use. The dose usually given was 5 cc.

intramuscularly. As much as 50 cc. have been given without especially unpleasant symptoms. In Hirschfelder's cases, 10 were permanently cured by one injection, 6 by two and 2 by three injections. In all of them, male and female, the administration of the extract was combined with local treatment so that the test was not a perfectly fair one. However, one patient, a girl of seventeen, with a cervical and vaginal gonorrhea of six month's duration, the discharges from both sources containing gonococci, was treated by gonococcic extract alone and absolutely no other remedy was employed. The injections were followed by rapid improvement and after five injections had been given during twenty-four days, the gonococci had disappeared. During two months on examination no gonococci were found. Hirschfelder thinks it seems reasonable to assume that when the gonococci are present in the urethra, any antibody which might form in the blood would have difficulty in reaching them and we had to be prepared for a failure of the remedy under such conditions. However, in systemic infections the results appear to be more favorable. Of seven patients with epididymitis treated, all but two recovered, the beneficial effects being rapidly produced. Seven other patients with gonorrheal rheumatism were treated with the extract and all have recovered and remained well.

Copelli (4) reports 84 cases of acute and subacute gonorrheal urethritis treated "solely" by vaccines with 64 cures; 32 cases of chronic urethritis with 31 cures; 27 cases of epididymitis with 26 cures; 5 cases of gonorrheal rheumatism all cured. Failures were attributed to the fact that the vaccines were not stable in composition. The value of complete rest in bed was emphasized.

N. P. L. Lumb (5), after treating a large number of cases of gonorrhea, conceived the idea that the only way of eradicating the disease was to attack it through the blood, in the same way as with arsphenamin in syphilis. He obtained good results in acute gonorrhea, administering at frequent intervals large doses of a mixed stock vaccine. However, in addition, weak irrigations of potassium permanganate and other local treatment were given. Lumb states the rationale of his method as follows:

(1) to effect the blood as early as possible with a view to (a) antagonizing the gonococcus; (b) diminishing the likelihood of complications. (2) To secure as great a reaction as possible in the shortest time without inducing a negative phase. Lumb refers to the work of Eyre and Stewart by which it has been proved that a gonococcal vaccine increases the power of the blood to destroy the living organisms and that one positive phase can be superimposed upon another by giving suitable injections at the proper intervals, thereby obtaining the maximum effect. In utilizing this fact two main lines of treatment were adopted. (1) Intensive dosage with a mixed stock vaccine containing twenty million gonococci and fifty million staphylococci per cubic centimeter. (2) Weak urethral irrigations. Three injections are given within the first five days, the total number of gonococci injected in that period being sixty million and one hundred and fifty million staphylococci. It is believed that by adhering to this scheme a series of positive phases is actually imposed one upon the other, thus producing the maximum effect. Irrigation is commenced with a weak solution of potassium permanganate (1:8000) and then replaced by 1:6000. This strength is not to be exceeded without special reason. To the assertion that vaccines are dangerous in the acute stage and lead to complications, Lumb replies that if this were so a large proportion of complications would have developed from the start with big doses. This was not the case and the most remarkable feature of all was the exceptionally low percentages of relapses. Out of 500 cases 2 only have occurred during a period of four months after completion of the series. Many of the cases left the hospital more than six months ago. This gives a relapse rate of less than 1 per cent, which seems to be a very satisfactory proof of the value of the vaccines as a test cure.

In the treatment of gonorrheal arthritis, H. D. Haworth (6) reports good results from the use of sensitized gonococcal vaccines which have the advantage of being less toxic and can be pushed without causing local or general reaction. In his first case, in which an autogenous sensitized vaccine was given, improvement took place after failure of an ordinary autogenous

vaccine and also of a stock sensitized vaccine made from several strains of gonococci. The initial dose was one hundred million, this being gradually increased to a maximum of two thousand million given at intervals of four days. In 16 out of 17 cases of gonorrheal arthritis the treatment was successful.

D. Lees (7), early in 1916, while testing in a parallel series of cases of gonorrhea different modes of treatment, both local and general, was impressed with the results in a large series of cases obtained by a mixed vaccine which contained in each cubic centimeter one hundred and fifty million staphylococci and fifty million gonococci. Definitely noticeable were: (1) the mild course of the cases treated ab initio with vaccine; (2) the absence of complications; (3) the smaller number of relapses. In conclusion, Lees emphasizes, that every case treated with vaccines should be treated locally, the vaccine being used as a valuable adjunct to the treatment and the dosage of the vaccine regulated according to the serological results, and by close observation of the bacteriological process of the disease and the reactions obtained. Only thus can we do justice to this most valuable method of therapeutics in systemic gonorrhea, as in other infections.

CONCLUSIONS

1. Gonococcus vaccines in the treatment of acute gonorrhea are of negative value.

2. In gonorrheal complications vaccine therapy is of value, when considered in the light of an adjuvant to standardized treatment and not as a specific per se.

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STOPCOCK AND FITTINGS FOR ATTACHING CHISMORE EVACUATING BULB TO THE BUERGER CYSTOSCOPE¹

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The difficulty of dislodging fragments from vesical pockets, even with the Chismore evacuating lithotrite inspired the following simple device. Ready attachment of the instrument makes it possible to remove the elusive piece after having located it with the cystoscope and after having approached it as nearly as possible with the fenestra before withdrawing the telescope. With the bulb attached as shown in figure 3, pumping of the bladder is as easy as with the Chismore evacuating lithotrite.

Figure 1 shows the stopcock alone. Its length is such that the hand grasps it so that the little finger aids in supporting the sheath of the cystoscope, the thumb and index finger steady the bulb and bottle, while the middle and ring fingers straddle the stopcock, whose neck is made long for this special purpose.

The sheath end of the instrument fits on the outside of the hub so as to be made fast by the thumb-button clamp thus providing almost absolute rigidity. The bulb end has a smooth ground tapering nipple holding the bulb watertight and airtight. When the stopcock is opened the lumen is the same as that of the cystoscope sheath thus preventing fragments from becoming caught at narrow points.

Figure 2 is self explanatory and shows the stopcock assembled with the Chismore bulb and bottle.

¹ Presented before the Genito-Urinary Section of the New York Academy of Medicine on April 20, 1921.

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Figure 3 needs no further comment than its own demonstration of the entire instrument assembled, ready for pumping the bladder through sheath and stopcock into the bottle.

Of course when the bladder is being filled the stopcock is simply closed during the steps exactly as is done with the Chismore evacuating lithotrite.

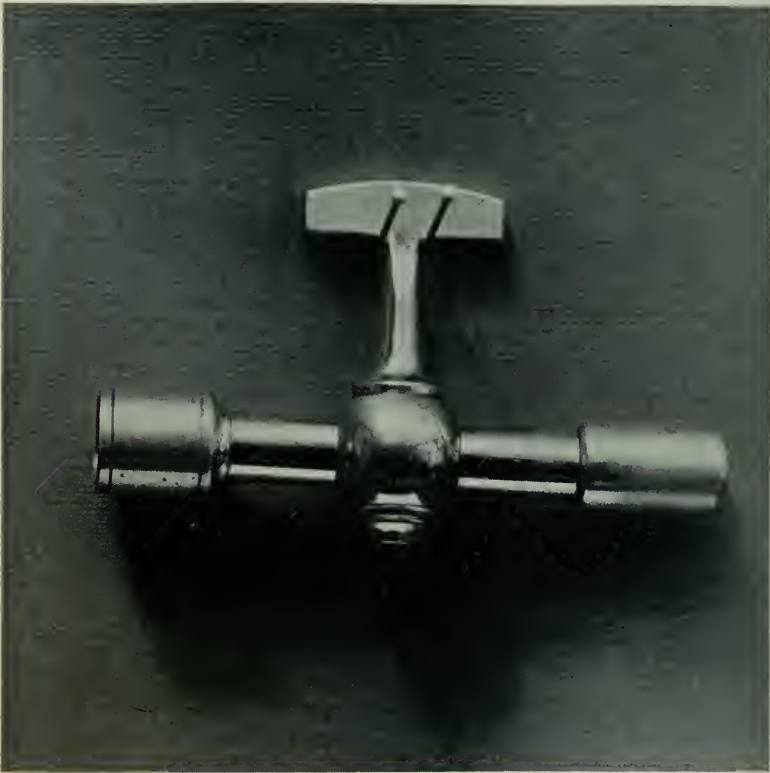


FIG. 1. PEDERSEN STOPCOCK: VALVE OPEN

Ordinary professional courtesy requires acknowledgment that the idea of this little device was borrowed from the stopcock attachment of the Chismore instrument.

I am indebted to Messrs. George Tiemann and Company for the production of this serviceable instrument, who write me



FIG. 2. PEDERSEN STOPCOCK WITH VALVE OPEN ATTACHED TO CHISMORE EVACUATING BULB AND BOTTLE



FIG. 3. BUERGER CYSTOSCOPE SHEATH (OLD MODEL), PEDERSEN STOPCOCK WITH VALVE OPEN ATTACHED TO CHISMORE EVACUATING BULB AND BOTTLE, COMPLETING INSTRUMENT FOR PUMPING THE BLADDER

that they made it in February, 1913. It is hoped that the service it has rendered to me will be found available for a large number of associates and friends. The effort will be made to have cystoscope makers standardize the hubs of their cystoscope sheaths so that this and any other similar attachment becomes universal and available for any make or type of instrument.

THE RELATION BETWEEN SPINA BIFIDA OCCULTA AND CERTAIN CASES OF RETENTION¹

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In the past five years I have encountered a number of patients suffering from a retention of urine that has seemed to depend upon an unusual type of interference with the normal innervation of the bladder. A study of these cases has seemed to point to the probability that this interference depended upon a spina bifida occulta.

I have called attention to this condition in a paper that I read before the Genito-Urinary Section of the American Medical Association in Chicago in June, 1918, and also in a paper that I presented at a meeting of the New York Branch of the American Urological Association in October, 1918. As I believe that this is a commoner condition than many have supposed, and one that deserves more study at the hands of the genito-urinary men, I am bringing it to your attention today. I shall report a few of the most definite cases that I have found though not all, by any means, that I have seen.

The first case of this sort that I recognized came to me in March, 1915—and has been described in my previous papers. She was a single woman, twenty-two years old who had been well up until she had come down with measles two years before. Since her measles she had had frequent and painful urination as well as a turbid and at times foul urine. Three weeks before I saw the patient she had what was apparently a very acute cystitis with bloody urine. Cystoscopy showed an acutely inflamed bladder with evidence of a mild pyelonephritis on both sides. I have no record as to whether or not she had a residual at this time, but two weeks later, after she had had her bladder at rest with a retention catheter, she had an eight ounce residual which gradually increased until three or four months later her bladder had a seventeen to eighteen ounce residual. A Wassermann was negative.

¹ Read at the meeting of the American Association of Genito-Urinary Surgeons, Rochester, Minn., May, 1920.

Two careful examinations made by a competent neurologist at intervals of some weeks failed to demonstrate any nerve lesion and the diagnosis of hysteria was made. As this patient carried a large residual urine, she was taught to catheterize herself and she got along fairly well. Shortly after this time an autopsy report on a former patient led me to have radiographs made of this patient's lumbar and pelvic regions and these showed an abnormality in the sacrum and coccyx that was quite in keeping with cases of spina bifida occulta as evidenced by such museum specimens of this condition as I could find. When I last heard of this patient some time later, her condition was not greatly changed—she was kept comfortable by regular catheterization. Figure 1. A drawing made from a radiograph shows pretty well the changes in this patient's sacrum and coccyx.

Case II. This case concerns an unmarried woman, thirty-one years old, who had in September, 1916, an attack of "sciatica." A year later another attack of the sciatic pain, accompanied by very obstinate constipation and bladder trouble, lasting a few weeks. In February 1918 she had to strain a great deal to urinate; after a time she began to have incontinence both during the day and at night. It was for this condition that she consulted me: she then said that she ordinarily felt no desire to urinate but did so at stated times because she knew that she ought—the urine was slightly turbid and she had a residual of 3 ounces. It was learned later from her family physician that she had had at one time a considerably larger amount of residual, between 8 and 10 ounces. There was a little irregularity in the region of the sacrum. Radiographs showed the vertebral canal was uncovered in the last two segments of the sacrum. This last occurs so often that in the absence of any evident abnormality it would be considered more as an unimportant anatomical variation than as a defect. This patient was examined by Dr. George L. Walton who could find some loss of sensation in the buttocks. He verified the provisional diagnosis of a lesion of the cauda equina, probably due to spina bifida occulta. In his opinion there was a paresis of the detrusor of the bladder and also of the sphincter due to involvement of certain fibers of the cauda.

This patient was referred to Dr. C. A. Porter for his opinion as to the wisdom of attempting some operative procedure; this he believed would be unwise. He called attention to the fact that there was a marked lack of tone to the perineal muscles which allowed one to feel the anterior wall of the sacrum for a much greater distance than usual. He also pointed out the fact that there was more of a defect on the front

of the sacrum than on the back—evidence that her spina bifida occulta was of the more unusual anterior type rather than the commoner posterior type. This patient was advised the regular use of a catheter and when last seen in September, 1919, was much less troubled with incontinence than she had been. She had at that time, however, a residual of 8 ounces of turbid urine. The radiographs of this patient are not typical. The open sacral canal is seen frequently when no lesion of the cauda is present. The change felt on the anterior surface of the sacrum is not evident in the radiograph. •

Case III. The following case is one that came under the care of Dr. C. A. Porter and he has kindly allowed me to make use of it. This man, thirty-five years old, appeared at the Massachusetts General Hospital in March, 1916. His story was that he complained of bladder trouble which had slowly and steadily been getting worse for a period of fourteen years. For three years he had been unable to control urination and defecation. The lack of control of the bowel was only partial; he was unable to control loose movements. When sneezing or coughing there was an involuntary escape of urine and his bladder muscle had no expulsive power; he depended entirely upon his abdominal muscles to empty his bladder. There was an area of anaesthesia in the sacral region supplied by the fourth and fifth sacral nerves, and also anaesthesia on the right in the region supplied by the third sacral. The right side of the scrotum was anaesthetic. By rectum one could feel on the anterior surface of the sacrum two rounded masses with a sulcus between them. They suggested to a certain extent a prostate which was projecting from the back rather than from the anterior surface of the rectum. The mucous membrane moved freely over them. These masses which were about the size of limes, did not fluctuate and evidently arose from the anterior wall of the sacrum. They were not tender but were somewhat elastic. The examining finger could reach above them. The urine was negative. Both sphincters were somewhat relaxed. There was no history of syphilis. A Wassermann of the blood was weakly positive; the spinal fluid was negative; a gold chloride test was negative; X-rays showed what was considered as probably a tumor or cyst involving the sacrum from the second to the fourth segments. This patient was kept under observation for something over a year and was given X-ray treatments on the possibility that his trouble was a very benign type of sarcoma. According to Dr. Porter there has been no improvement in this man's symptoms and no great progression. From the radiographs, of which

I have had a drawing, one may fairly assume that this case belongs to the same type of deformities as those previously reported. The bony deformity is greater in degree than in any of the other cases.

Case IV. The last case is one that has not been reported previously; it is that of a single woman twenty-seven years old, who entered my service at St. Elizabeth's Hospital in June, 1919. Her story was that she had had trouble voiding urine ever since she could remember. Three years ago she had an attack of cystitis since which time she has had pain on voiding gradually getting worse. She has been in various hospitals and while local treatment has always made her better the trouble has always returned when she gave up treatment. Examination showed a thin woman, reflexes normal with the exception of some diminished sensation about the general region of the anus. Her urine was turbid and foul, almost to the extent of having a fecal odor. Various observations showed a residual that varied from 5 to 7 ounces. There was a slight tuft of hair in the sacral region: this is almost pathognomonic of spina bifida occulta. On either side of this tuft of hair there was a little white scar. A certain amount of deformity of the sacrum could be felt externally and likewise there was some change in the anterior surface of the sacrum as felt through the rectum. The patient was given bladder washings and then allowed to go home. She was to report later for operation but has not done so. The X-ray showed a condition that I believe is without doubt a spina bifida occulta. A drawing made from the X-ray gives a fair idea of the bony deformity.

I could add further cases to the list but the reported ones are as typical as any I have had and I believe illustrate the condition well.

It may be contended that the condition seen in these cases is more like a cyst of the sacrum and coccyx than like a spina bifida occulta. In the last case this certainly cannot be so. The tuft of hair, and the scar coincide exactly with the typical spina bifida occulta as described by Virchow. The other three cases with the exception of the tuft of hair, present pretty much the same appearance as this case, both as regards the X-ray and as regards the symptoms. It seems to me that we have reasonable evidence to assume that the condition in these cases is spina bifida occulta and not a cyst of the sacrum.

Spina bifida occulta was recognized by Virchow in 1875 and described minutely by von Recklinghausen and Fischer in 1886,

and also by Ribbert at a somewhat later date. Attention was called to most of the earlier cases by the presence of a tuft of hair over the region of the sacrum, a condition to which Virchow called attention. It is said that the presence of this mass of hair always means a spina bifida occulta, but on the other hand it is by no means present in all cases. Some cases have shown a diffuse lipoma over the sacrum, others a naevus or a bit of pigmented skin. Still others have shown a fine white scar or perhaps a deep coccygeal fossa. In some instances one finds none of these signs but simply feels a little depression in the sacrum. Radiography has shown a distinct sacral defect in many of the cases recently described, but a large number of the cases reported in the literature antedate radiography.

A word of caution is needed lest one puts too much importance on defects in the laminae of the lower part of the sacrum. One finds that imperfect roofing over of the sacral canal in its lower segments, the fourth and fifth more especially, is common. One finds this low median defect not infrequently in persons who have no evidence of spina bifida occulta. These low sacral variations, if one may call them such, become suggestive of spina bifida occulta only when they are associated with evidence of defective innervation in the region supplied by the sacral nerves. These defects may be indicated by motor, sensory, or tropic disturbances.

Some have held that spina bifida occulta represents the scarring and contraction that follows the intra-uterine rupture of a spina bifida cystica; others that it is simply a lesser degree of the same defect without hernia of the cord or its covering. The bony defect is due to failure of the tissues of the mesoblast which forms the bony and muscular coverings of the cord to push in between the epiblastic tissues that form the spinal cord itself, and that part of the epiblast which forms the skin. This closure of the vertebral canal begins above and ends below. Defects that involve the sacral nerves, those that have to do with interference with the function of the bladder are more common than defects higher up. They are also less often associated with severe motor and trophic disturbances, and it is probable that they are somewhat more susceptible of help. It is likely that

the failure of the bone to fuse depends in part at least upon an increased intra-spinal pressure due to some intra-cranial inflammation. This may account for those relatively rare cases where the spina bifida is anterior and would seem to depend upon direct pressure from within rather than upon any developmental failure.

The symptoms presented by ordinary cases of spina bifida *cystica* have varied considerably but have usually shown marked sensory and motor disturbances of the lower extremity. Club-foot, ulcers of the foot, and similar trophic disturbances have been common. Urinary disturbances have not been as common as these other manifestations and when they have been reported have usually been instances of incontinence rather than of retention. Some of these cases of incontinence however may well have been the incontinence of an overdistended bladder. Some of the cases that have shown incontinence of urine have also shown a lack of complete control of the rectum. As compared with the cases of spina bifida *cystica*, the cases of spina bifida *occulta* seem on the whole to be accompanied by rather lesser nerve lesion; the sensory, motor and trophic disturbances of the lower extremities have been less common than in the cases of spina bifida *cystica* and the urinary lesion has been retention rather than incontinence.

These cases that show retention, seem to represent in a way a lesser lesion than those with incontinence. This is borne out in case II in which the retention came first and then as the disease progressed was followed by incontinence. I believe in this patient there was at first a paresis of the detrusor with consequent retention and then at a later time there occurred a paresis of the sphincter with consequent incontinence. Since the incontinence was not complete, it would suggest the partial paralysis of both the detrusor and the sphincter. The fact that this patient rarely feels any desire to urinate but simply tried to void at stated intervals because she knows she should, would seem perhaps to speak for some interference with the sensation of the bladder. With this patient there were no reflex changes to be obtained on examination, only indications of nerve changes

consisted in abnormal sensation over the region of the buttocks. In most of my cases that have been examined by neurologists the motor and sensory changes have varied so little from the normal that the neurologists have doubted the existence of any lesion of the cauda. This I take to mean that in these cases, I refer especially to the ones with retention, the nerve changes are so definitely confined to the fibers that supply the bladder that no other abnormal sensory or reflex changes are present.

In many cases of spina bifida occulta the symptoms pertaining to the bladder have appeared early in life as in case IV. In other cases they have appeared late, as in the other three cases I have described. It may seem rather unusual that a condition that was present at birth should not show symptoms early in life. This probably depends on several factors: one is that the spinal cord extends much lower in the vertebral canal in intra-uterine life than it does later:—in adult life the cord ends, and the cauda begins, about the level of the second lumbar vertebra. If any of the fibers of the cauda are attached to the scar tissue filling-in the bony defect in the vertebral canal, there may be no interference with their function until there has been a considerable tension on these fibers; this tension is due to the increasing disproportion in length between the cord and the vertebral canal which takes place in adult life. The mass of fatty, fibrous tissue that fills the bony defect in some instances of spina bifida occulta apparently increased in size as time goes on until it exerts an injurious pressure on the cauda. Then too, this late involvement of the spinal nerves may be more apparent than real. In cases showing retention, this retention and consequently the nerve lesion that caused it may have existed for a very long time before it gave sufficient symptoms to attract attention. Such cases of this sort, as I have seen, have only been recognized after the bladder has become infected and I believe that in these cases, as is the case for instance in cases of diverticulum of the bladder, the condition may go on for a very long time without symptoms unless the bladder becomes infected. It may very likely be, that the interference with the bladder innervation and therefore, bladder function, may have antedated the appearance of symptoms by a very long time.

The mechanism of the retention in these cases is probably an interference with the nerve supply of the detrusor due to a pulling or to a pressure upon fibers of the cauda which results in a partial paralysis of the muscle. Because of the way it is brought about, its intensity and the disturbance it causes may vary markedly. It is possible that some interference with the function of the sensory nerves of the bladder may play a part as in the second case I reported where there was an absence of any feeling or desire to empty the bladder. I should not suppose that any lack of coordination entered into the mechanism of this type of retention.

As the cause of the retention in these patients is probably due to a mechanical interference with fibers of the cauda, it is useless to look for permanent relief by any means other than attacking the problem mechanically at the point where the interference has taken place. Operations carried out for the relief of symptoms caused by spina bifida occulta in general have consisted either in dissecting out the fatty, fibrous mass pressing on the cord or cauda or in separating the nerve fibers that are attached to the scar that fills the bony defect in the vertebral canal. Usually this is followed by a plastic to close the defect in the bony canal. These operations have not been as a whole very satisfactory, but they have occasionally given remarkable results. They seem to be attended with neither the mortality nor the discouraging results that have attended most operations upon cases of ordinary spina bifida cystica. It would seem probable that the earlier these operations were carried out, the more hopeful the outlook for the restoration of the bladder function. In some of the cases of long duration a pressure myelitis has developed. This is probably a very late result. Of course no improvement following operation could be expected if this change had taken place. Of the cases reported in this paper none has been operated upon; one previously reported had what seemed to me to be an inadequate operation, that gave no relief.

I believe that this condition of spina bifida occulta will be found to explain certain very perplexing and trying bladder conditions, and I trust further that a more accurate knowledge will show the way to treat the condition successfully.

PRIMARY CARCINOMA OF THE MALE AND FEMALE URETHRA¹

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In view of the rarity with which carcinoma is met with in the male and female urethrae and the errors which have been made in the diagnosis in a number of the comparatively few reported cases, it has seemed worth while to the writer to again call attention to this unusual but important group of cases; to put on record two cases recently met with; one in a man from the genito-urinary service at the Massachusetts General Hospital, the other a woman from the writer's private practice, together with some previously unreported cases from the Massachusetts General Hospital records; and also to attempt a brief review of the more recent literature and, for the sake of convenience, to add the references to some scattered cases not included in the tables of cases so far reported.

Primary carcinoma of the male urethra is a rare condition and as a rule has received but scant attention in the various text books on genito-urinary surgery. Thomson Walker in his book "Genito-Urinary Surgery," published in 1914, gives an account of the condition and refers to two of the most complete monographs on the subject, one by Hall, 1904, and a later one by Preiswerk in 1907. The most recent publication that I have found is by Tanton in 1910 in the *Gazette des Hopitaux*. Preiswerk collected from literature 42 cases. The tables of Hall contain 6 cases not included by Preiswerk. Barney reported in 1907 2 cases from the Massachusetts General Hospital. Walker mentions 3 others of his own. To this list I can add a case reported by A. T. Cabot in 1895, 1 by Peacock in 1910, 1 by Minard in 1910, 1 from the Massachusetts General Hospital

¹Read at the meeting of the American Urological Association, New York, April, 1920.

records 1913, making a total of 58 including the following recent case which entered the Massachusetts General Hospital.

Husky, white male, sixty-four years old, single, a furniture-mover, visited the Out-Patient Department complaining of:

Frequency, day, 8-10, night, 1-8, for several years.

Difficulty of from one to five minutes in starting micturition for six months.

Pain, dull and uncomfortable, between penis and rectum, gradually increasing for six months.

Burning micturition and burning in the rectum for ten days.

Malaise and discomfort had prevented work for twelve days. Temperature was 99.4°. White blood count was 16,400. There was a mass in the perineum and a large reducible right inguinal hernia. He was referred to the Hospital with the diagnosis: Periurethral abscess.

Past history. "Grippe" for two days, two weeks before entrance. Ruptured vastus externus, ten years ago. G. C. infection, thirty-five years ago.

Physical examination. Large man with flushed face. Thirsty. No palpable adenopathy. *Heart* negative. *Lungs*: Both sides full of coarse moist râles and squeaks, no areas of dulness.

Abdomen. Large reducible right scrotal hernia. Relaxed left ring. Bladder dulness about one-third way up to umbilicus.

Rectal. In perineum is a large uniform tumor, the size of one's fist, extremely tender, and very hard. By rectum patient is exquisitely tender. Bladder is easily felt, apparently distended. Prostate not made out. Anterior wall of rectum seems very firm.

Reflexes. Normal.

Extremities. Large varicose veins of both legs, worse on the right.

Blood-pressure. Systolic, 128; diastolic, 78.

Urine. Clear, alkaline; specific gravity, 1.020; trace of albumin; no sugar. Sediment shows 10 pus cells per high power field.

Wassermann. Negative.

Non-protein nitrogen. 36 mgm. per 100 cc. of blood.

Treatment and results. Attempts to catheterize with soft rubber catheter, unsuccessful. Slight debris on end of catheter, when withdrawn. Obstruction, apparently at swelling in perineum. Hot Sitz bath, ineffective.

Operation. Excision of specimen from perineal tumor. Suprapubic cystostomy for acute retention. No pus was found in the perineum. Urethra could not be catheterized. Through the perineal incision, a hard brittle mass was felt about the bulbous urethra.

Post-operative. Patient lived for a month, during which: perineal wound healed partly; urine drained freely from clean suprapubic sinus, and dribbled a little from the urethra; patient suffered with moderate pain in the penis; the right leg and thigh grew large and edematous. During the last two weeks patient grew continuously weaker, his lungs were full of râles, he ran a picket-fence type of temperature, 103° on the peaks each day, pulse about 120, and respirations increased steadily each day until they were 50. He died twenty-six days after operation.

Surgeon's note. "A most unusual case of primary cancer of the urethra. No demonstrable involvement of prostate or bladder. Symptoms resembling periurethral abscess and extravasion of urine, and diagnosed and operated upon as such. . . . Kidneys unimpaired."

Pathological report on specimen from operation: "Small piece of firm tissue showing a grayish white, fibrous surface on section. Microscopic examination shows irregular columns of atypical cornified epithelium in a well developed fibrous stroma. Diagnosis: Epidermoid Carcinoma."

Dr. Cabot's case reported in 1895, but not included in any of the collected tables, is briefly as follows:

C. W. T. Entered March 29, 1895. Elderly man entered hospital complaining of:

Painful swelling in the perineum, nine weeks duration; incised and drained of pus.

Flow of urine through incision; spread of perineal tumor and increase of outflow.

Past history. G. C. thirty-five years before entrance. Perineal abscess nine years before entrance.

Physical examination. Indurated mass in the perineum, extending forward beneath the scrotum with two fistulous openings in it. Urethra, impervious to smallest instruments, which were arrested at the peno-scrotal angle.

Operation. April 1, Perineum opened widely. Pus excavated from many side pockets. Walls, sloughing. Drainage tube placed in cavity and brought out in front of scrotum.

Post-operative. Part of induration cleared up, but there still remained a hard sloughing mass at the bottom of the cavity about the urethra.

Operation. Two weeks after the first; exploration and biopsy. "Hard tissue, distinctly of the nature of a neoplasm, extending forward to peno-scrotal angle and backwards to a point just anterior to the triangular ligament." Prostate, not abnormally large.

Pathological examination. "The bulk of the fragment is composed of large solid masses of rather small, slightly cylindrical epithelial cells, separated by a relatively narrow stroma of vascularized connective tissue. The central parts of the epithelial masses, which have a more or less branching character, have undergone necrosis."

Diagnosis. Cancer of the urethra.

The other case previously unreported from the Massachusetts General Hospital records is as follows:

E. J. B. Entered September 25, 1913.

White male, married, farmer, aged fifty-one, entered hospital complaining of:

Pain on pressure in the penis for two months.

Difficulty in starting stream for two months.

Creamy urethral discharge.

Painful erections.

Past history. Indefinite history of partial retention for many years. Circumcised to improve this, eighteen years before entrance. Urethral discharge off and on for eight years.

Physical examination. General physical, not significant. Lungs: numerous coarse moist râles.

Genitalia. Profuse creamy discharge from urethra. Smear positive for G. C. About half way down penis, apparently surrounding urethra, is a hard annular, non-tender mass.

Rectal. Moderately enlarged prostate.

Operation. Periurethral section for stricture urethrae.

Post-operative. Patient discharged twelve days after operation with a granulating wound, through which he passed small amounts of urine. Urethra took a No. 28F sound and functioned well.

Readmitted one month after discharge now complaining of: *Leaking* through the perineum; *pain* in the perineum.

Physical examination. Urethral discharge and perineal fistula with exuberant granulations. In front of the fistula is a tender indurated area in the bulb. Rectal; negative. Sounds pass out through the perineum. Temperature 99.2°.

Diagnosis. Periurethral abscess and perineal fistula.

Operation. Incision and curettage of abscess walls. Tissues about sinus found to be very boggy and necrotic.

Post-operative. During the two weeks following operation, local condition did not improve and a mass surrounding the anterior urethra to the perineal opening was noted as extending into bulbous urethra and anteriorly.

Secondary operation. Area of induration laid open and found to be sloughing cancerous looking tissue. This surrounded the urethra from the bladder to the middle of the scrotum.

Post-operative. During the two weeks following patient grew progressively weaker, and tumor and pain in the perineum increased. Discharged home to die, one month after last operation.

Pathological examination. A portion of the urethra with a thickened velvety surface and with a firm base. Microscopical examination showed a plexiform mass of large flat epithelioid cells with many imbricated whorls infiltrating the tissue in all directions.

Diagnosis. Epithelioma.

In the majority of the cases the lesion arises from the bulbous portion of the urethra. The following two cases are of interest in that they began in the penile urethra. Peacock's case was a man of seventy with obstruction to micturition, the growth being situated 1 inch from the meatus involving the urethra. Partial amputation of the penis was performed with good results. Pathological report showed cancer beginning in the urethral gland. Minard's case was one involving the meatus and fossa navicularis. Amputation of the penis was performed with dissection of the inguinal glands.

From the age of the reported cases the disease rarely occurs before fifty. In Hall's table there is one case of twenty-two and four between forty and fifty. Among the predisposing causes trauma is mentioned, also leucoplakia resulting from chronic urethral irritation. Stricture is present in a good many of the cases, more than 50 per cent, but it is difficult to reconcile this condition with the etiology when one considers the great frequency of stricture and the rarity of carcinoma. In some cases there is no venereal history whatsoever.

In the majority of the cases the bulbous urethra is the seat of the neoplasm. The growth spreads along the mucous membrane, destroying it and invading the corpus spongiosum, later the periurethral tissue becomes invaded and abscesses and fistulae supervene, opening in the perineum or scrotum, occasionally in the pubic region, buttock, and rectum.

In advanced cases the perineum may be the site of a bulging ulcerated mass. The penile urethra is less often affected, but carcinoma has been found originating in the glands near the meatus and along the urethra. It sometimes spreads from here to the bulbous portion. The inguinal glands are often involved. The growth takes the type of squamous epithelial cancer.

Unfortunately the early symptoms are not characteristic of the malignant nature of the lesion and are generally such as would coincide with the ordinary urethral stricture. Urinary symptoms are most often met with, increasing difficulty and frequency of micturition, with or without attacks of acute retention. Hematuria, hemorrhage from the urethra and a purulent discharge occur. These, of course, are met with in ordinary stricture of the urethra.

As the disease advances a swelling appears in the perineum, simulating periurethral abscess or infiltration, and extravasation of urine. On incision the true character of the lesion may be discovered but not infrequently it is not until a second operation is undertaken for lack of closure of the fistula or relief of the supposed stricture after drainage of an abscess, or the wound has taken on an appearance suggestive of malignant disease, and a section of tissue removed shows its true nature.

The case herein reported was typical in history and examination of urethral stricture with abscess, but no pus was found on incision, instead a brittle cavity surrounding the bulbous urethra, the tissue removed showing carcinoma.

The diagnosis in the penile portion offers less difficulty here, a gradually increasing swelling and induration about the urethral wall or at the meatus, with a narrowing of the canal.

Syphilis is to be excluded by the Wassermann test and failure to respond to active treatment. The age of the patient is sugges-

tive. The growth has in some cases been demonstrated by the urethroscope.

As has been said the diagnosis from stricture with extravasation or fistulae is extremely difficult and at times impossible without operation, and unfortunately the rarity of carcinoma is such that suspicion is not easily aroused. As a rule the perineal swelling is out of proportion to that seen in ordinary stricture, but here again this varies within wide limits. The "wooden" induration of the tissue about an old urinary sinus may be very suggestive of malignancy. I recall such a case where a diagnosis of cancer was made, but the section removed at operation proved to be a chronic inflammation only.

In none of the three cases here reported was the diagnosis of cancer made previous to operation, one of them not until a second operation was performed and in another not until a third was done. This case was complicated by an acute gonorrheal urethritis. The primary diagnosis in each case was stricture with abscess.

In regard to treatment unfortunately when first seen many of the cases have become so far advanced as to be inoperable, except for local drainage or relief of urinary retention by perineal or suprapubic drainage.

In some of the earlier cases resection of the bulbous urethra has been attempted. Oberlander reports such a case where there was no recurrence for four and a half years, but at the end of this time the growth reappeared in the prostatic urethra. Total emasculation has been performed. Of ten cases treated by resection or some form of extirpation collected by Hall, the result is unknown in one. Of the remaining nine, death occurred in four within nine months, while one had a recurrence in six months. In the other four there was said to have been no recurrence in 21, 11, 10 and 4 months respectively. From this it will be seen that the results are far from brilliant. Nevertheless extirpation should be tried if the growth is diagnosed early. Amputation of the penis has given good results in the early cases involving the penile portion of the urethra only. I have found no reports of the use of radium in this condition.

While the disease is of rare occurrence its possibility should always be borne in mind by the surgeon when confronted with an indurated mass in the perineum in a man of over fifty, as its recognition has a very important bearing on the prognosis and treatment.

Primary carcinoma of the female urethra is also a rare lesion but probably not so uncommon as the paucity of cases found in the literature would lead one to believe, as doubtless many cases have not been reported. The text books up to very recently have treated the subject but slightly as in the case of carcinoma of the male urethra. Thompson Walker's "Genito Urinary Surgery" 1914, Kelly-Burnham's "Diseases of the Kidneys, Ureters and Bladder," vol. ii, 1914, and Cabot's "Modern Urology," vol. i, 1918, give more or less attention to the subject. In 1903 Percy collected from the literature 16 cases, in 1908 McMurtey added 10, Manton in 1910 collected 35, the next year 1911 Whitehouse reported 43 and in 1914 Watson added 8 more from literature and a case of his own, making 52. In 1910 Gibson reported a case before the American Association of Genito Urinary Surgeons which has been overlooked in the reported tables. Since that time a few articles and case reports have appeared. Legueu and Stark each report a case in 1914. Crosson, 3 cases in 1915, Shoemaker, 1 in 1916. To these I can add my own case and 8 others from the records of the Massachusetts General Hospital, making a total of 68 cases.

My own case is as follows:

Woman, sixty-two, married. Seen in consultation with Dr. E. C. Cood of York Harbor, Me., April 15, 1919.

Complaint. Difficulty and pain on micturition for five years. Has been getting worse of late. Great pain and difficulty at present time. Eleven years ago operated on for some uterine trouble. Hysterectomy? Five months later an operation for gall stones. Four to five years ago an operation for the removal of a growth from the urethra probably a carbuncle. Since that time has had the urethra dilated at various times. Has lost 25 pounds during the last few months.

Examination. Woman in fair general condition. The vaginal outlet is contracted. There is some irritating discharge which is at times

bloody. There is an indurated mass involving the posterior wall of the urethra extending laterally on each side and extending as far as the bladder neck. The calibre of the urethra is diminished, the surface uneven and eroded and bleeds easily. Examination very painful. Glands in right inguinal region enlarged.

Cystoscopy. Urine slightly cloudy. 1015 acid, albumin trace, sugar none. Sediment pus. The bladder is involved about the internal meatus more so on the right.

The general condition of the patient was such that radical removal of the entire urethra and resection of the bladder with permanent suprapubic drainage or possibly reimplantation of the ureters was not advised and treatment with radium was recommended. She received four applications at the Huntington Hospital on April 28, May 17, June 12, July 4 of respectively 45 minutes, $\frac{1}{2}$ hour, $\frac{1}{2}$ hour and 1 hour. After the second and third treatment there was some improvement in the symptoms, urination becoming easier and less painful for a while. There was no change locally however except for some sloughing of the growth. After the last treatment she became worse, was unable to get about, lost strength and weight rapidly and died from cachexia in September, 1919.

Although no pathological examination was made, clinically there is no doubt but that this was a case of primary cancer of the urethra taking its origin probably from the caruncle which was present four or five years previously.

The following 8 cases briefly from the Massachusetts General Hospital records are of interest only in regard to the symptoms and diagnosis and in that a pathological report is given, there being no record of the end results. But 3 were operated on.

1. E. K. Entered April 9, 1889. White female, married, aged fifty-three, entered hospital complaining of:

Soreness. In region of uterus for four months—quite severe at times. (Two weeks ago, cervix was dilated, which started profuse, thin offensive discharge, but relieved the pain.) “Bunch” in the vagina for two months. *Hematuria*, and partial suppression.

Physical examination. Well developed and nourished. Good color. Good pulse. Temperature normal.

Ether examination. Vagina showed nothing. Cervix, hard, with a small tight os. Whole vestibulum occupied by new growth, size of

plum externally, ragged, ulcerated. Considerable discharge with apparent leaking of urine. Urethra opens into lower part of tumor. Fragment snipped and sent for diagnosis. Inoperable.

Surgeon's note. Inoperable.

Discharged, after three days.

Pathological examination. Masses of flat epithelial cells separated by bands of connective tissue.

If this is destructive in nature, that is evidently going into the tissue, it is cancer; if not, a papilloma.

Diagnosis. Cancer around the meatus urethra.

2. B. H. Entered January 21, 1890. White female, married, aged twenty-nine. Entered hospital complaining of:

Tenesmus of bladder. *Frequency*, twenty times a day.

Past history. Abscess of the labia, ten years ago. Operation on growth of the urethra, one and one half years ago, and again four years ago; portions removed.

Physical examination. Meatus urinarius completely obliterated by a cauliflower-like growth, which is opalescent on the surface, and red on separation of the folds.

Operation. Clitoris, meatus urinarius, etc., which were affected by the growth, excised.

Discharged after uneventful convalescence of ten days.

Pathological examination. A papillomatous and ulcerating mass surrounding the urethra. Section showed very much thickened layers of flat epithelial cells, but in the deeper tissues were found infiltrated masses of swollen flat epithelial cells.

Diagnosis. Epithelioma.

3. M. O. Entered June 21, 1892. White female, aged sixty-five, housewife, entered hospital complaining of: *Incontinence, itching, burning, loss of weight, constipation.*

Past history. Always delicate. Indigestion.

Physical examination. Fairly well developed and nourished. Pale. At meatus is some induration and swelling but no well defined tumor. There is occasional hemorrhage. Urine, that of mild cystitis.

Operation. Urethra dilated to 40F. Vagina packed with iodoform gauze.

Post-operative. For one week after operation patient was quite incontinent. Discharged two weeks after entrance with good control. "Still has pain."

Diagnosis. Carcinoma at meatus urinarius.

4. R. D. Entered May 12, 1892. White female, widow, aged fifty-two, housekeeper, entered hospital complaining of:

Difficulty and pain in passing water, increasing for six months.

"Heaviness" in the vagina.

Pain, dragging, along inner side of right thigh; pain like burning knitting needles in bladder.

Bleeding from urethra, after straining to void, off and on for three months, lately every second day. Large hemorrhage from urethra, causing her to feel faint, night before admission. Not confined to bed. No loss of weight.

Physical examination. Ulceration within the meatus; whole urethra and periurethral tissues infiltrated with hard nodular growth, extending almost to base of bladder. Mass, size of a man's thumb. Enlarged glands felt on deep pressure in iliac fossa. Small glands, in both groins. General condition good. Residual urine, 8 ounces.

Notes. During twenty-two days in hospital, patient had to be catheterized every four hours. No hemorrhage seen. Ulceration increased; foul smelling discharge appeared on the 17th day. Rubber catheter could not be passed. Silver catheter met with considerable resistance and a ridge near bladder? Discharged with bougie catheters to use.

Diagnosis. Cancer of urethra.

5. J. P. White female, fifty-five years old, married, entered hospital complaining of:

Tumor in region of right labium for ten weeks; and in region of left labium for six weeks.

Frequency of urination for eight weeks, growing steadily worse.

Hematuria, twice during the last ten weeks.

Pain, considerable, constant in suprapubic region, which was relieved by urination.

Loss of appetite and strength.

Constipation.

Past history. Nothing important.

Physical examination. Fairly well developed. Considerably emaciated. *Heart*, Slight enlargement to the left, and harsh systolic murmur on the left side. *Lungs*, negative. *Abdomen*, dulness over the upper abdomen; in suprapubic region is a round soft elevation, suggesting a distended bladder.

Per vaginam. Both labia prominent, not edematous; between fingers placed on each labium is felt a hard mass, just within vagina, beneath pubic arch, more extensive on right of median line than on left; not especially tender. Patient in distress apparently from retention.

Treatment and results. Catheter passed with difficulty, and 12 ounces of urine withdrawn, with relief. Slight bleeding from urethra afterward.

Urine. Normal color; alkaline; specific gravity 1.009; slight trace of albumin; sediment; few leucocytes, few fresh red blood cells.

Notes. Patient remained in hospital thirty-eight days, during which time she had considerable suprapubic pain, apparently due to retention and relieved by catheterization. On the eighth day, temperature was elevated to 101° and left labium was more swollen, red and tender than usual. Otherwise chart was negative. Temperature, 99°; pulse, 75; respiration, 25.

Physician's note. "As disease seems very extensive, operation not deemed advisable. Patient therefore discharged."

Diagnosis. Malignant disease of urethra.

6. J. B. Entered February 18, 1902. White female, married, housewife, aged fifty-two, entered hospital complaining of:

Urgency for many years; day 5-6; night 1-2.

Pains, smarting and shooting, about the urethral meatus during urination and when walking, almost every day for two years. Tenesmus, occasionally.

Family history. Mother died of phthisis. Father and two sisters have "diabetes."

Past history. Not remarkable except operation one and one-half years before entrance for urethral caruncle, failed to relieve. *Bleeding*, occasional and slight, since operation.

Physical examination. General examination not remarkable. *Local:* Edges of meatus urinarius hypertrophied, forming a projecting tumor, size of a pea, with meatus in the centre. Posteriorly is a reddened denuded area of mucous membrane from the centre of which projects a small comb of granulation tissue. Very tender. Slight erosion on right side of meatus. Uterus normal. Erosion of the cervix, with a small papilomatous growth on it the size of a pea.

Urine. Acid; albumen, 0; sugar, 0.

Operation. Excision of urethral caruncle. Plastic on the posterior wall of meatus. Trachelorrhaphy.

Notes. Remained in hospital for five days after operation, during which smarting at the meatus was the only symptom. Wound healed well except for slight reddening at the posterior edge of the meatus. Chart, normal. Discharged well, on eighth day after entrance. Two weeks after, felt much better. Examination about the same.

Pathological examination. A small piece of granulated looking tissue which on microscopic examination showed solid masses of rather large, irregular epithelial cells infiltrating a round cell tissue which was quite sharply differentiated from the very vascular fibrous tissue.

Diagnosis. Cancer.

7. M. O. Entered April 27, 1903. White female, married, housewife, forty-two years old, entered hospital complaining of:

Pain, burning, and sharp and stabbing, in nature, before, during and after micturition for eight months.

Tenesmus. Vesical, for six months.

Sore at urethral meatus for five months.

Bloody vaginal discharge every day for five months.

Loss of weight. Ten pounds in last six months.

Past history. Not significant except: Two months before entrance sore at meatus was scraped at Homeopathic Hospital and some tissue removed. Discharged, feeling better. Advised to have X-ray treatment.

Physical examination. General physical, not remarkable, save for pallor and signs of moderate emphysema. *Local:* Anterior and posterior walls of vagina are involved by an indurated growth, somewhat ulcerated, bathed in pus, and continuous with ulcerated mass which involves the urethra. Cervix is free from growth.

Discharged after nine days in the hospital with slightly elevated temperature and pulse, and normal respirations.

Diagnosis. Inoperable cancer of the urethra with extension to vagina.

8. K. C. Entered October 14, 1914. White female, married, aged 47, housekeeper, entered hospital complaining of:

Frequency every half hour for six weeks.

Pains, as of bearing down, and drawing sensations in the vagina.

Loss of weight considerable.

Family history. One maternal aunt died of cancer. One sister had growth removed from vagina, ?carcinoma. History otherwise not significant.

Past history. Measles in childhood. Pulmonary tuberculosis three years ago. Sanitarium treatment for ten months. Discharged, cured eight months ago. General health good since.

Physical examination. General physical examination negative, save for dulness and râles in both lungs. *Local:* In the position of the urethra is an excavated area with indurated walls, with complete de-

struction of the whole urethra to the bladder neck. The ulcerated area is firmly adherent to the pubic arch and upper one-third of the pubic rami. The base of the bladder and anterior vaginal wall behind the bladder neck, feel normal. Cervix in normal position; not lacerated or eroded. Uterus freely movable.

Surgeon's note. The condition clearly represents a carcinoma of the urethra with involvement of the neighboring vaginal wall. It is believed possible to remove the growth after exclusion of the urine by double ureterostomy.

Operation refused. Discharged unrelieved with the diagnosis of cancer of the urethra.

Of the etiology of carcinoma of the female urethra little can be said. All writers on the subject have laid stress upon the rarity of the lesion in a region so prone to injury and chronic irritation, generally supposed to be a factor in the development of malignant disease. As in the male leucoplakia is given as a predisposing cause. That caruncle is a forerunner in some cases there seems to be no doubt, my own case having been previously operated on for that supposedly.

In the histological examination of 19 tumors removed under the clinical diagnosis of caruncle at the Massachusetts General Hospital in twenty years Young found tissue suspicious of malignancy in 5. That is a high proportion, but again caruncle is a very common disease of the female urethra.

The microscopical examination of the excised specimen shows squamous epithelioma to be by far the most common type of growth. Columnar epithelioma has been reported a few times. Pure adeno-carcinoma is more uncommon. It is thought to originate in the peri-urethral glands.

The clinical types are best described by Whitehouse and are quoted from his article as follows:

The cases are divided into vulvo-urethral and urethral.

Vulvo-urethral growths are by far the more common. In my series of 43 cases, 32 undoubtedly come under this category. From a careful revision of the literature I am of the opinion that three definite clinical types may be recognized.

(1) An irregular dark purple papillomatous growth, which bleeds readily on contact, and which may be mistaken for a simple polypus or caruncular condition of the urethral orifice.

(2) An ulcer, produced by the breaking down of a nodule on the floor of the vestibule at the urethral orifice. The ulcer presents the usual malignant characters, having a hard indurated, irregular margin and friable, sloughing base. It rapidly involves the whole of the vestibule and spreads to the labia minora.

(3) An induration surrounding the urethral orifice leading to depression, puckering and contraction of the orifice itself, but free from all ulceration and proliferation. This appears to be of slow growth and clinically is a scirrhus.

Urethral growths are distinctly rarer and only 11 are included in the list attached to this paper. Here again, two modes of growth may be recognized.

(1) An irregular, elongated ulcer, involving the mucous membrane of the urethral canal, and only exposed by urethroscopic examination. The ulcer is usually situated on the floor of the canal in the distal segment. It has the usual malignant characters and tends to extend towards the urethral orifice. It rarely involves the bladder. The case described by the author is included under this group.

(2) A peri-urethral induration, but free from ulceration until the late stages. A definite tumour is formed, which tends to occlude the urethral canal, and which involves the whole length of the urethra. This type is of slow growth and approximates to the scirrhus. In its later stages ulceration occurs in the vagina, urethra or vestibule.

It will be noted, therefore, that in all types of growth the last stages are similar, and in an advanced neoplasm it is impossible to say whether it was originally vulvo-urethral or primarily urethral.

Extension takes place through the inguinal and pelvic lymphatic glands.

The condition rarely occurs before the age of fifty although cases are reported at a much earlier age, Watson's case being twenty-seven, Legueu's twenty-six, and one of McMurty's twenty-six. It is most common in the decades between fifty and sixty and sixty and seventy.

There are practically always urinary symptoms, difficult, frequent and painful micturition, haematuria, or bleeding and

discharge from the urethra. Retention of urine from obstruction may occur. Pain is generally a prominent symptom and may be very extreme in some cases. In others it is not marked.

The diagnosis should not present any particular difficulties and by a careful examination should be made early in most cases, as the symptoms are such as to cause the patient to seek relief. At least it should be made or excluded when the patient does present herself, and although rare, the possibility of malignancy should always be borne in mind in any growth or induration in or about the urethra. In moderately advanced and advanced cases it is perfectly obvious. Syphilis primary and tertiary are to be excluded as well as simple caruncle or a benign tumor which may or may not have become ulcerated. In all cases where doubt exists a piece of tissue should be removed for microscopical examination.

In the advanced cases when infiltration of the tissues has occurred operation other than a palliative one for drainage of the bladder is useless.

When the growth is confined to the urethra radical removal should be attempted and some surprisingly good results have followed this procedure. In general the technique consists of making an incision about the urethral orifice including all the diseased tissue. The dissection is then carried up under the symphysis pubis well up to the bladder neck by traction on the growth and the urethra amputated through sound tissue and the edges sutured to the vaginal mucous membrane. Urinary control is maintained to a surprising degree in many cases. Cresson modifies this technique somewhat by using a purse string suture to pucker up the muscular tissue about the urethra at the bladder neck, and the employment of preoperative drainage by means of a vesico vaginal fistula which is closed later if it does not heal spontaneously.

When the growth involves the bladder neck and incontinence would result from removal, it is better to close the wound at the bladder outlet and make a permanent suprapubic fistula. McGill has employed a suprapubic opening to push the growth down towards the vulva where it was excised, the wound healing spon-

taneously and the patient having a permanent suprapubic fistula.

Cresson has collected the results in 25 cases which were subjected to a more or less radical excision. Of the cases traced about half were apparently cured, which is quite encouraging. Some of the operations were not very extensive being excisions of one-half or one-third of the urethra, a strong plea for early diagnosis and operation.

Of the 25 cases:

Cures (three years).....	8
Probable cures (two years).....	3
Recurrence known.....	8
Result not known.....	6

One of these cases had no recurrence at the end of nine years (Vineberg); one, none in four years (Boyd); and a third free at the end of six years (Peterson).

I have not been able to find very much on the results of radium treatment of cancer in this location. It was certainly of no value in my case.

Lequeu in 1914 reports an interesting case in a girl of 26 where the disease was very advanced and judged inoperable but complete disappearance of the growth followed the use of radium. Six treatments were given of five hours each externally without much improvement. Later radium was introduced into the urethra. The ultimate result was a cure. There was involvement of the labia and incontinence of urine. Microscopic examination showed the growth to be squamous epithelioma. Thirty months after the disappearance of the cancer, ureteral implantation into the bowel was attempted to cure the incontinence of urine at the patient's request as she wished to be married. Death occurred eight days later from peritonitis. Autopsy showed no recurrence.

Shoemaker in 1916 reports a case in a woman of fifty much benefited by radium. She had complete retention. The urethra was hard and indurated like a pencil from the meatus to the bladder. The urethral orifice was retracted and nodular. Nine applications of three hours each with 20 mgm. of radium element were employed. The patient disappeared considering herself well.

Watson advocates the use of radium after operation to render recurrence less likely and cites a case where it was so employed. A total of 600 mgm. hours to the vulva and 150 mgm. hours to the groins were used.

Kelly and Burnham advise the use postoperatively of massive doses of radium bromide 500 to 1000 mgm. for from twelve to twenty-four hours well shielded and brought into intimate contact with the affected part.

The literature of the subject has already been alluded to in part. As regards cancer of the male urethra it is scanty. The earlier cases have been collected and tabulated by Hall (1904) and Prieswerk (1907) in admirable papers. Since then I have found cases reported by Peacock, one, (1910), Menard, one, (1910), and A. T. Cabot, one in 1895. These have been briefly abstracted here and a little more fully two previously unreported cases from the Massachusetts General Hospital. These with a long article with an extensive bibliography by Tanton 1910, two cases reported by Barney in 1907 and three mentioned by Thompson Walker in his book in 1914, compose all that I have been able to find on the subject.

The literature on carcinoma of the female urethra is more voluminous. One of the best recent papers is by Watson who quotes the previous writings on the subject by Percy, McMurty, Manton and Whitehouse and adds some references bringing the subject up to 1914. That same year Stark describes an operative procedure and reports a case. Crosson in 1915 made a study of the results in 25 operated cases, and gave in detail a technique which he had developed and employed adding three personal cases. Lequeu in 1914 and Shoemaker in 1916 each report a case where radium was used with success although in the latter case the diagnosis was clinical and the end result unpublished.

A list of the important publications since 1908 is added for convenience.

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TUBERCULOSIS OF THE KIDNEY COMPLICATED BY IMPACTED PELVIC CALCULUS¹

H. A. FOWLER

Fortunately the occurrence of true stone and tuberculosis in the same kidney is rare. The differential diagnosis between renal lithiasis and renal tuberculosis, while relatively simple in many cases, may be extremely difficult or impossible without exploratory operation.

Among the methods employed in modern urologic diagnosis, roentgenographic examination is undoubtedly the most valuable in differentiating between the two conditions. The shadows which are seen not infrequently in tuberculous kidneys, due to the deposit of lime salts in the caseous areas, are confusing, and may be easily mistaken for those of true stone and lead to an error in diagnosis. However, the occurrence of multiple shadows, widely scattered within the kidney area, the absence of uniform density, and their irregular contour, will usually lead to a correct interpretation.

That true stone and tuberculosis does at times occur in the same kidney is shown by a recent observation in which the stone was impacted in the pelvic ureter, causing complete obstruction. The case history is briefly as follows:

On February 24, 1920, I saw in consultation with Dr. Ruffin, Mrs. L. W., aged, thirty-seven years, who entered the George Washington Hospital on February 18, complaining of pain in the right kidney region and right iliac fossa. The following history had been obtained: Father died at fifty-two years of Bright's disease. Mother died at thirty-seven years of typhoid fever. Two brothers, aged twenty-seven and thirty-three years, are in good health. One sister is well except for a persistent headache for the past two years. There is no history of tuberculosis, cancer, syphilis, gout, rheumatism, or other hereditary disease.

¹ Read at the meeting of the American Association of Genito Urinary Surgeons, Rochester, Minn.



FIG. 1. SMALL STONE IN LEFT KIDNEY (SECOND RECURRENCE). LARGER STONE IMPACTED IN RIGHT PELVIS
PRODUCING COMPLETE OBSTRUCTION

Past history. The patient was a delicate child. She had diphtheria at two and again at seven years of age. There were no complications or sequellae. The period of adolescence was notably one of health. At the age of twenty years she began to suffer with pain in the left kidney region. The diagnosis of renal colic was made at that time. These attacks recurred at intervals of three to five months. At the age of twenty-one years an X-ray examination showed a stone in the left kidney. In February of the following year, 1905, a stone was removed from the left kidney by Dr. Geo. Ben Johnson, of Richmond.

She was married in 1907, at the age of twenty-four years.

Ten years after the first operation, May, 1915, she was operated upon by Dr. Moore, of Alexandria, and a stone the size of a bean was removed from the same (left) kidney. Two years later, March, 1917, she was examined by Dr. Hagner at the Garfield hospital, Washington. Both ureters were catheterized, and an X-ray examination was made of the kidneys. A stone was found in each kidney, the larger one being on the right side. Three months later, while in Richmond, she was seized with a severe attack of pain in the right side which was diagnosed renal colic. Returning to Alexandria she was operated upon for appendicitis and a healthy appendix removed.

In October, 1918, she had influenza, during the epidemic of that year. Following her recovery from this, she had repeated attacks of colic requiring morphia to control. She was treated by a chiropractor, who gave spinal massage. At this time she began to lose weight. During the next six months she lost 25 pounds.

In July, 1919, while at the sea-shore, she was suddenly seized with a sharp pain in the right kidney. Thereafter she was unable to lie prone on account of pain which was relieved only by being propped up with pillows. She returned to Alexandria the following September, suffering with severe pain in the right hypochondriac region. An X-ray examination at this time showed a stone in the right kidney. In November she had a severe attack of colic, localized in the right kidney. She was treated by a homeopathic physician for a time, and finally consulted Dr. Ruffin.

Habits. No irregularities or excesses in mode of living. She has never been pregnant. Her usual weight is 150 pounds. She now weighs 126 pounds. Her present illness is a continuation of her previous illness. During the past three months she has been suffering with a dull pain in the right kidney and the right iliac fossa.

During the first period of twelve days that she remained in the hospital, the temperature ranged between 97° and 99.8° running a mildly septic course. Examination of the blood gave a red cell count of 4,200,000, leucocytes 15,000, haemoglobin, 60 per cent. The urine



FIG. 2. EXTENSIVE DESTRUCTION RIGHT KIDNEY BY TUBERCULOSIS. THE STONE IS SEEN LYING FREE IN THE PELVIS

was clear, persistently alkalin, of normal gravity, and repeated examination showed only an occasional red cell, a few leucocytes, and triple phosphate crystals. Tubercle bacilli were never found in the urine. Physical examination showed nothing of note except a mass in the

right upper quadrant of the abdomen. The report of an X-ray examination, made on February 21, is as follows: Examination of the gall-bladder region shows no abnormality. Examination of the urinary tract shows two shadows of calcified bodies; one on the right side and one on the left. The one on the left side is about the size of a navy bean, and is probably a stone in the pelvis of the left kidney. The one on the right side is about three cm. long and 1.5 cm. wide and is on a level with the third lumbar vertebra and close to it. This has the appearance of a stone in the right ureter, or possibly in the pelvis of an enlarged and displaced right kidney. There is an indefinite shadow on the right side which may be that of a much enlarged kidney. Final diagnosis in this case should be made after catheterization of the ureter (Christie).

Such were the data obtained previous to our visit. Examination of the abdomen showed a large mass in the upper right quadrant, firm but elastic, smooth, and not very tender. It reached the mid-line in front, extended slightly below the level of the umbilicus, and disappeared beneath the right costal border. Tympany was present over the mass in front. On bimanual examination it was slightly but definitely movable. It was thought to be an enlarged kidney, but the exact nature of the swelling was not apparent.

Double ureteral catheterization with X-ray catheters was done. The left catheter passed easily to the pelvis, and clear urine was obtained, free from infection but containing a few red cells, and corresponding in character to the catheterized bladder urine. The right catheter passed a distance of 26 cm. meeting an impassable obstruction. No urine could be obtained from this side. An X-ray examination was made with the cystoscope and catheters in place. The plates show the tip of the left catheter close to the stone which is undoubtedly in the left pelvis. The tip of the right catheter passes along side the stone for a distance of about one-half its vertical diameter where further progress was arrested.

It was apparent that the stone on the right side was producing complete obstruction of the right ureter at its junction with the pelvis. As no secretion could be obtained from this side, we were unable to determine the nature of the tumor, but it was unquestionably connected with the right kidney.

Operation, March 9, 1920. At operation the stone was readily felt deeply behind the greatly enlarged kidney. While palpating the stone, it slipped suddenly away from the finger, upwards into the pelvis. The

mass was then freed from its bed, delivered, and excised. It was not until the greatly enlarged and manifestly diseased kidney was excised and sectioned that we had a clue as to its pathology. It presented multiple typical tuberculous abscesses, involving the pyramids. These abscesses were filled with thick pus and caseous material. There was no deposit of lime salts. The stone, previously felt, was lying free in the pelvis. Convalescence was unusually smooth and rapid. The patient left the hospital on the thirteenth day, with the wound solidly healed.

The pathologist reported as follows: There is almost complete destruction of the parenchyma with a pronounced granulomatous increase of the connective tissue elements. Sections show masses of chronic tuberculous granulation tissue with considerable necrosis among which are many ill-defined tubercles. In the most distal parts of the cortex a few glomeruli and uriniferous tubules are present, but all show considerable round cell infiltration and encroachment of the tuberculous process. All the tuberculous mass is apparently encapsulated, no perinephritic tuberculous lesions being found.

Remarks. This is the first instance I have observed of renal tuberculosis complicated by a true stone in the same kidney. I assume the condition is unusual and relatively rare. In this case the fact that the stone was impacted, producing complete obstruction of the ureter, adds further interest from the standpoint of diagnosis. By reason of the occlusion we were unable to obtain any secretion from the right kidney, and were unable, therefore, to determine the nature of the tumor mass before operation. The real pathology was not suspected until the excised kidney was examined.

The calculus was the size of a large bean, greyish white in color, with a rough surface.

It appears most probable that the calculus formation preceded the infection with tuberculosis. We know, for instance, that three years previously examination by X-ray and ureter catheter showed a calculus in the right kidney larger than the recurrent stone on the left side. This calculus had doubtless been present for a considerable time. The symptoms at that time were those of renal lithiasis. No mention is made in the history of tuberculosis having been found or even suspected. There had been no bladder symptoms, and none developed later. It is more than likely that infection of the bladder would have occurred from an

active focus in the kidney in a much shorter time. It was seventeen months after this examination that she is said to have had influenza and began to lose weight rapidly. It is probable that infection of the kidney with tuberculosis occurred at this time. Impaction of the calculus doubtless occurred nine months later with the onset of the severe symptoms suggesting occlusion of the ureter. This probably accounts for the fact that the bladder escaped infection as well as the rapid destruction of the kidney by the tuberculous infection.

I have made no search of the literature for the report of cases of renal calculus and tuberculosis occurring in the same kidney. In his chapter in *Modern Urology* O'Neil says, "While undoubted instances of simultaneous occurrence of renal calculus and renal tuberculosis, and the development of renal tuberculosis in a kidney previously the site of calculus, are found in the literature, the conditions are rare." In 256 cases of renal calculus and renal tuberculosis reported from the records of the Massachusetts General Hospital, no cases of true calculus were found in tuberculous kidneys as opposed to the calculous deposits, nor were there any cases of the development of tuberculosis in kidneys from which calculi had been removed (O'Neil).

In their paper on *Roentgenographic Diagnosis in Renal Tuberculosis*, Braasch and Olson state that "Actual stone formation is rare in tuberculous kidney. When it does occur it is generally a phosphatic stone, formed in a localized abscess with necrosis and secondary infection. . . . It may be inferred that primary stone formation is unusual in patients with renal tuberculosis."

FURTHER CLINICAL STUDIES ON THE USE OF MERCUROCHROME—AS A GENERAL GERMICIDE

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Since the publication in 1919 of our preliminary laboratory and clinical study of "Mercurochrome 220"¹ (1), this compound has been used extensively in many urological conditions in the Brady Urological Institute and in other genito-urinary and gynecological services and dispensaries. The satisfactory results in urological practice have led to its application in other branches of medicine and surgery where a deeply penetrating, non-irritating germicide of low toxicity and relatively quick action is desired. As a result of our experience with this drug over a period of two years, we believe that our early expectations of its great value have been realized. In many cases it has proved effective where other drugs have failed, and there have been cases where the reverse was true. It is no more a panacea for urinary infections than is any other disinfecting agent, but it is unquestionably a valuable addition to the comparatively few powerfully germicidal substances which can be applied to sensitive surfaces such as the mucosa. Since our first publication several articles which show the value of Mercurochrome in many different branches of medicine have appeared.

LITERATURE

In ophthalmology it has been used extensively in infections of the cornea and conjunctiva, due to the gonococcus and to other organisms. "A Clinical and Laboratory Report on the

¹ Hereafter the use of the number 220 will be dropped, and in this paper Mercurochrome will be abbreviated to M.

Use of Mercurochrome in Ophthalmology" (2) was made by Lancaster, Burnett and Gaus before the Section of Ophthalmology at the New Orleans session of the American Medical Association. They reported only a limited number of cases treated, but the results were such, in their opinion, as to warrant a more extended use of this drug in ophthalmological practice. The laboratory tests conducted to determine the activity of M. in the presence of tears, mucus and pus gave germicidal values which corresponded very closely to the values given by our tests of this compound in the presence of urine, serum, etc., due allowance being made for difference in diluent and medium and difference in technique.

In the discussion of this paper, Travis (3) reported several severe cases of chronic streptococcus infection of the middle ear in which he had secured remarkable results by the use of M. after the failure to secure results with other drugs used over long periods of time. Since that time, in a personal communication, Dr. Travis has reported marked success in long-standing and refractory cases treated by the local use of this drug alone. Later its use in middle ear and mastoid infections was advocated by Callison (4) who reported satisfactory results achieved by its use.

In the treatment of ophthalmia neonatorum Clapp and Martin (5) report that M. has proved to be very efficacious, and publish reports of a number of cases in which it was used with good results.

DeWitt (6), experimenting with the action of certain organic mercurial compounds, found that M. inhibits the growth of the tubercle bacillus completely at 1:5000 and partially at 1:10,000. These dilutions are 50 and 100 times the average dilution recommended for intravesical use. M. in 10 per cent solutions, but not in less concentrated solutions, kills the tubercle bacilli in twenty-four hours so that they will not infect guinea pigs. These laboratory findings naturally suggest the use of M. solutions in the tuberculous ulcerating lesions of the genital tract.

Mercurochrome successful in curing chronic diphtheria carriers

Gray and Meyer (44). "In searching for a germicide, we had to consider the enemy we were engaged against, knowing full well his predilection for hiding places in crypts of the tonsil, between the folds of the mucous membranes, in erosions, ulcers and also behind any shelter he can find in the nasal and pharyngeal passages. The report by Young, White and Swartz,(1) therefore, on the uses of the new germicide, lauding the marked penetrating and germicidal properties of that drug, and demonstrating that it can be utilized in relatively concentrated solutions on the mucous membranes of the bladder and urethra without causing irritation, gave us the suggestion to use this germicide in an attempt to reach diphtheria bacilli in the nose and throat.

"Of our total number of carriers we were able to treat, consecutively, thoroughly and systematically, only 90.

"Eighty-eight of our 90 carriers treated with Mercurochromes were made carrier free with an average of only 19.1 treatments, or applications of the germicide, with an average of but 12.7 sick days. The two extra sick days (19.1 treatments approximating 10 days) resulted from one day in the hospital without treatment before his last culture had been made, and another day passing before we were able to obtain the result of this final culture. The remaining two of the 90 carriers resisted all our efforts as they continued to harbor the bacilli in tonsillar crypts and in the scars of a peritonsillar abscess. One of these two was even treated by having him lie on his side, flooding the tonsillar area with a 2 per cent solution of M., and retaining it there for ten or fifteen minutes, but without avail. We finally had to resort to tonsillectomy in this case. This patient's nose, which was also positive (a clinical case), cleared up relatively early under the use of M, but the throat, although we obtained an occasional negative culture, consistently remained positive.

"The 1 per cent solution of M. was used as a routine application by means of a medicine dropper, spray or swab. In the more resistant cases we used the 2 per cent strength, and in cases showing any evidences of congestion or irritation, we used the 0.5 per cent strength. When persons complained of the application of the drug by means of the nasal swab, we used the medicine dropper and had them hold their heads back for a minute or two after the application, until the drug passed back into the nasopharynx. We relied on the medicine dropper

in the nasal tract almost entirely and on the swab for the tonsils. In patients with nasal obstructions we utilized the nasal spray as a means to have the germicide reach the organisms.

"In addition to systematizing the treatment of diphtheria carriers, we have found that the germicide of choice is a solution of M. in 0.5, 1 or 2 per cent strength. By using this drug we were able to obtain in our series of carriers of diphtheria bacilli 88 carrier-free persons, following an average of 19.1 applications of this solution, with an average of only 12.7 sick days, as compared to an average of twenty three days, the best results we have found recorded for a large number of carriers."

Use of mercurochrome in dentistry

Darnall (8). "The high germicidal power of M. coupled with its lack of irritating effect and its thorough penetration made it particularly suited to oral pathological conditions.

"In gingivitis and stomatitis the treatment used was practically the same for both. The membrane is dried and protected by use of cotton rolls, and the area touched with a 3 per cent solution of M. In infected sockets the socket is washed out with a strong antiseptic spray, all necrotic tissue removed, and the solution carried down into the socket with a small pledget of cotton.

"In pyorrhea, after prophylaxis, the teeth are isolated with cotton rolls buccally and lingually, and the surface dried as much as possible. The solution is carried down into the pocket with a small wisp of cotton wrapped on a broach. Care should be taken to protect the crown of the tooth from staining.

"In root resection, after curettement, the cavity is touched with a 3 per cent solution of M. In putrescent root canals it is our belief that this germicide will prove to be as efficient as any used in this branch.

"This drug is especially suited to the treatment of gingivitis and stomatitis. A 3 per cent solution was used with impunity in all open lesions, no irritation resulting. The best results are obtained by drying off the part affected and applying the solution not oftener than every other day."

Reports by letter or in person

In order that we might not be carried away by "the lively expectation of important results which is the cause of such

exaggerated estimates of the therapeutic values of new remedies," we sent a questionnaire to a number of physicians and surgeons to whom we had previously sent a supply of M. for clinical trial, asking for their opinion of its therapeutic value in the conditions in which they had used it.

Replies were received from twenty physicians who had used this product in their clinical work. Their reports are abstracted and included in this paper for the clinical data submitted to us. Wherever details were given in the case histories, the cases were incorporated in our tables. The attached tables give results of the questionnaires and the replies received.

We wish to express our thanks to Surgeon-General Ireland for reports received from the various army camps and hospitals and to the fine spirit of cooperation in the medical corps.

It is scarcely necessary to call attention to the great difficulty of securing reliable, accurate data of clinical results in the treatment of urethritis, both specific and non-specific, in our general dispensaries. A large majority of the cases do not cooperate with the physician, and a still greater percentage discontinue treatment just as soon as annoying symptoms such as pain and discharge have disappeared.

Drs. Scott and O'Malley, working in the United States Public Health Venereal Clinic at Mercy Hospital, Baltimore, found the stain caused by M. to be very serious objection to its use in acute gonorrhea in public dispensaries. The stains are easily removed from the hand and skin by the use of acid alcohol, vinegar, permanganate and oxalic acid solution, sweet spirits of nitre, Dakin's or Harrington's solutions, but stains on the clothing are more persistent and may present tell-tale evidence of a condition which the patient does not care to have known. As we anticipated early in our work with M. we have found the stain to be a serious objection to its use by the patient.

Laboratory tests. The work of Swartz and Davis (9) established the fact that solutions of M. in a strength of 1:16,000 will kill the gonococcus in twenty minutes in vitro; 1:800 M. solution in urine kills *B. coli* in one minute, whereas 1:100 acriflavin requires one hour to kill *B. coli* in urine. In 50 per cent dog

serum M. 0.5 per cent kills *B. coli* in one minute, whereas acriflavin 0.5 per cent fails to kill *B. coli* in one hour.

Acute urethritis. Solutions of 1 per cent are as a rule well tolerated by the urethra, and we have used as high as 5 per cent solutions in the urethra in some instances. Occasionally, a 1 per cent solution may prove to be irritating and a weaker solution must be employed. This is in accord with clinical experience in the use of any antiseptic in the urethra. In our work, complaint of burning other than a temporary smarting has been very infrequent. It is our opinion that solutions of 0.25 to 0.5 per cent are sufficiently concentrated to produce a satisfactory germicidal effect in the urethra and are always non-irritating. Emphasis should be laid on the desirability of using fresh solutions, as Swartz and Davis have shown that the solutions deteriorate on standing.² In spite of the high test tube germicidal activity of these solutions, the results obtained by local use of these solutions in acute gonorrhea have not been vastly superior to those obtained by the intelligent use of other drugs. The introduction of the water soluble sodium salt and the abandonment of the use of the alkali soluble form of the drug is responsible for a diminution in the amount of irritation produced by these solutions. Excess of free alkali proved irritating to the mucosa of the urinary tract. Cases reported in our first paper (1) were treated with solutions made from the alkali-soluble dye. Cases reported in this paper were all treated with the later water-soluble compound. The stain led a number of patients to discontinue treatment and has been a factor in preventing the accumulation of accurate clinical data

² This drug which is a bisodium salt of dibrom-oxymercury fluorescein was originally prepared in our laboratories in the Brady Urological Institute as the free acid soluble in the theoretical amount of alkali. Although the preparation of the solution in this way was quite satisfactory under chemical control, it was not suitable for use by the average physician, and we had reports of irritation, due, doubtless, to the presence of excess alkali. Later, Messrs. Hynson, Westcott & Dunning, Baltimore, prepared a satisfactory water-soluble sodium salt. Germicidal tests on solutions of this salt have shown that it is equal in germicidal value to the earlier alkali-soluble form. The preparation and chemistry of the drug have been presented elsewhere. (E. C. White: Mercury Derivatives of Phthaleins. Jour. of the Amer. Chem. Soc., 42, 2355 (1920)).

as to the germicidal efficiency of the dye in vivo. In acute gonorrhea (100 cases) we were able to render the urethral discharge microscopically free from organisms in an average of 16.8 days, and in a great many cases no gonococci were found after the first week. The length of time necessary to render the discharge organism-free depends, within certain limits, on the frequency of treatments and on the length of time the drug is retained in the urethra. In some of the cases, the treatments were often four days apart, while in others they were given several times a day, by which technique the best results are obtained. M. should be continued several days after the gonococcus has disappeared. Then gradually discontinuing the use of the drug in these cases and substituting copious hot irrigations of weak permanganate, silver nitrate or acriflavine, the discharge ceases and early cures are effected. M. has shown up as an excellent agent for injection in gonorrhea, but the deep penetration of the gonococcus into urethral glands and prostate make quick sterilization difficult for any drug. In cases seen in the first 24 hours, very quick cures have been obtained. We have not seen any stricture formation that we felt was due to the drug such as has been described after the use of other antiseptics. We have not seen the severe reactions reported to us by Kleiner (10).

Chronic urethritis. In the treatment of the chronic infections the value of M. is that of a quick-acting, penetrating, non-toxic and non-irritating germicide of great power. The most satisfactory results obtained by the use of M. in the urethra were in chronic urethritis. Used as an instillation and combined with needed instrumentation the results have been very satisfactory. This with but few exceptions is the consensus of opinion of the men who replied to our questionnaire. Very satisfactory results were also reported in non-specific urethritis.

In chronic posterior urethritis, associated with chronic prostatitis and vesiculitis, its beneficial action has been clearly demonstrated. We have recovered the dye from the prostatic secretion, obtained by massage, more than a week after its injection into the urethra. The purulent secretion expressed by

massage two or three days after injection is often stained a deep pink. Our procedure in these cases was as follows: The urethra was irrigated and the bladder was filled with sterile water, normal salt or weak permanganate solution. The prostate and vesicles were massaged and stripped. The bladder was then emptied by voiding and the M. solution placed in the posterior urethra by means of a Keyes posterior instillator, or forced back into the prostatic urethra by small hand syringe (rubber bulb type).

Roberts (11) reports having obtained the dye from the seminal vesicles two weeks after its injection into the vas (vasotomy) in cases of chronic seminal vesiculitis. Cumming (12) also reports very satisfactory results with this treatment.

In non-specific urethritis Grantham (8) reports prompt sterilization of the canal by the use of a 2 per cent solution retained for ten minutes, three times a day.

Cystitis. The results obtained in many cases of old, long-standing cystitis have been very remarkable. As is to be expected with the use of any antiseptic in this location and in the various types of infections, we have failed to eliminate the infection and render the urine germ-free in a certain number of cases, in some of which we have found the prostatic secretion infected and in others the kidneys.

While there is some difference of opinion as to the irritating qualities of the drug, and as to its value in acute infections, there is practically unanimous agreement as to the great value of M. in chronic infections of the urinary tract, especially those due to *B. coli*. Various observers report the clearing up of some of these old cases with a few instillations of 1 per cent solutions. These cases are usually due to colon bacillus. The drug does not yield such striking results when used in the coccus infections of the bladder or kidney pelvis. This clinical finding is in agreement with laboratory results recently obtained by J. H. Hill, bacteriologist to the Brady Institute. In a 50 per cent serum medium M. has been shown to be more effective against *B. coli* than against *Staphylococcus aureus*. The former is killed in one minute by a 1:200 dilution of the drug but not by a dilution of 1:300. To kill *Staphylococcus aureus* under the same conditions,

a dilution of 1:50 is required, showing a ratio of 4:1 in favor of *B. coli*. In exposures of one hour in the same medium *B. coli* is killed by a dilution of 1:600; *Staphylococcus aureus* by 1:200. We have seen no bad results from its use, but occasional cases complain of burning; these are the exceptions to the rule. We formerly thought that the presence of residual urine was a contra-indication to the use of M. We have since used it in cases with large residual, with no irritation and with good results, i.e., complete sterilization. We do not know why a 0.5 per cent solution should prove to be irritating in an occasional patient and not at all irritating in most other cases. We feel that the preliminary irrigation of the bladder with sterile water or normal salt solution to cleanse the bladder is essential. The solutions of M. should then be injected into the bladder and retained as long as possible. This may be repeated as often as three times a day, depending on the tolerance of the patient. As the object is to sterilize the bladder quickly, at least two treatments daily should be given if possible. It is best to begin with a weak solution, 0.5, and increase the strength of the solution to 1 per cent in a day or two, though in many cases two injections of 1 per cent solution daily are well borne. Solutions should be made fresh and kept in colored bottles as there is some deterioration in solutions kept a long time, with consequent loss of germicidal power.

There has been a marked relief reported in cases of tuberculous cystitis treated by daily instillations of M. We have not seen any cases where cure was obtained in tubercular cystitis by its use.

We have not seen any toxic symptoms, nor have we had reports of such, produced by the use of M. solutions in the genito-urinary tract. We have not seen any complications which we felt might fairly be ascribed to the use of the drug. In some cases the rapidity with which a foul purulent cystitis of long-standing becomes sterile and the urine clear and free from pus is remarkable.

Pyelitis. A large number of cases of pyelitis were treated with M. The incomplete records prevent accurate statistical studies

as to the relative efficiency of this drug and of silver nitrate which is in common use. As a result of our experience, we feel that M. has about as great a germicidal action in the renal pelvis as 1 per cent silver nitrate solution, and has the added advantage of not producing the painful reaction usually noted after the use of the silver solution. A reaction following pelvic lavage with M. is rare in our experience. We have not seen any evident toxic symptoms produced by its use. In resistant cases, the use of M. alternately with silver nitrate solution seems to be efficacious where results cannot be obtained by the use of either one alone. As many cases of "pyelitis" are due to foci of infection elsewhere (teeth, tonsils, etc.), cures are often impossible from pelvic lavage alone.

An objection to the use of M. in the kidney is the persistence of the stain which may interfere with the colorimetric reading of the phenol-sulphonephthalein output. The technique used in pelvic lavage is that described in our former publication (1).

Venereal ulcerations. Venereal ulcerations (chancroids, buboes, etc.) almost without an exception, when dressed with M. (either the solution or the paste) promptly become cleaner and the granulations healthy looking. Bowman (14) reports less contraction after healing of ulcers which have been treated with M. Buboes dressed with M. gauze heal very rapidly, and the period of disability is materially shortened. The results obtained are splendid, the only objection being the stain.

Other uses of M. Randall (15) uses M. to keep operative wounds of the genitalia sterile, and Healy (16) used it on vulvar ulcerations with good results. Baca (34) reports unusually good results obtained in carbuncles which had resisted the use of Dakin's solution for a prolonged period. When the cavities were packed lightly with gauze saturated with M. there was an immediate cleaning of the wound and a rapid healing.

Used instead of tincture of iodine to prevent infections in shop injuries, M. is proving very satisfactory in industrial surgery (De Hart) (18). It does not irritate the epidermis and inflammatory reaction disappears.

Chronic discharging sinuses. We have found M. particularly valuable in discharging sinuses, especially those following removal of tuberculous kidneys or epididymes. We also have reports from sanatoria for tuberculosis attesting its value in various forms of discharging sinuses and fistulae. A 1 per cent M. solution may be injected gently into a fistula with impunity daily. Its low toxicity and the escape of the excess fluid makes it much safer than bismuth paste in the treatment of deep sinuses.

ABSTRACTS OF CLINICAL RESULTS OBTAINED BY OTHER
OBSERVERS

The following are abstracts of reports and letters sent in answer to our questionnaires as to the results obtained with M.

Keaney (19). A report from United States Naval Hospital at Brooklyn, covering about ten weeks use of M. states that the results in the treatment of acute gonorrheal urethritis by the injection of 1 per cent and 2 per cent solutions four times per day have been most satisfactory. The purulent discharge gradually ceases in from seven to ten days and the smears become negative in about the same time. No complaint was made of irritation and the stain of the dye seemed to be the greatest objection to its use. Very good results have been obtained in treatment of chancroids by immersion of sore in 1 per cent M. for fifteen minutes every two or three hours.

Klingensmith (20). A report from Major Klingensmith at the United States Army General Hospital No. 41 gives results with M. in 27 cases of chronic gonorrhea. The hospital records did not permit of great elaboration, and detail; 20 cases were cured, 7 cases were not cured. Average number of treatments per day per patient, 2 to 6. Average number of days for a cure, 25. Average number of days the 7 uncured cases were treated, 34. These 27 cases were all chronic, and all had been under treatment for long periods of time, with other agents, acriflavine and protargol. No preliminary irrigation was used. Patient was required to void before the injection of M. No details as to complications, irritation, etc. given.

Bowman (14). A report of 20 cases of acute gonococcus infection of the urethra, both anterior along and anterior and posterior, treated by the hand injection of 15 M. twice a day, was received from Major

Bowman of Camp Meade. The urethral smears became organism free in from eight to fifteen days (average time not given). One per cent solution proved to be somewhat irritating and strength was reduced to 0.5 per cent, which proved to be non-irritating. Details of treatment not given, but report states no complications developed during treatment.

Five cases of chronic cystitis due to colon bacillus infection were treated by bladder irrigations of 1:500 solution of M. alternating with the instillations of 30 cc. of 5 percent solution M. into the bladder. The results were very remarkable. None of the patients complained of irritation or burning. There were no toxic symptoms. The urine became negative and bladder free from infection in from five to ten days (average not given). There were no recurrences in this series. In genital ulcerations due to chancroidal and mixed infections, 1 per cent and 2 per cent pastes were used as a dressing. The results were excellent all the sores immediately cleaning off and healing in from six to twenty days, without contraction or complications. Major Bowman also used gauze saturated in M. to pack suppurative chancroidal buboes with very prompt healing and no contraction.

Anderson (21). Lieut. Jas. K. Anderson, M.C., U. S. A., reported in full detail 13 cases treated by the use of M.; one acute anterior gonorrhea, 8 chronic gonorrheal urethritises cases, 2 tubercular pyelitis cases, 1 prostaticorrhea, and 1 verumontanitis. His acute gonorrheal cases were promptly cured, as were three of the chronic cases. Five of the chronic cases were improved but not cured at time report was sent in. One case of tuberculous cystitis was improved by the use of M-220. The other case was not appreciably benefited by its use.

Skeer (22). Skeer reports 60 cases treated with M., 36 of these were acute anterior infections only, 14 were acute anterior and posterior infections, and 10 were chronic anterior and posterior urethritis cases. He was able to render the urethral discharge free from organisms more quickly with M. than with the silver protein compounds and secured his best results in the acute cases. In this series the discharge was rendered organism-free in from five to twenty-four days. The average time was not given, nor were complications developing during treatment listed or failures given. His method was as follows: Four urethral injections of 1 per cent M. were given daily, the solution being retained from three to five minutes each time. The injections were preceded always by urination to cleanse the urethra. Severe cases associated with edema and swelling were not given local

treatment until the acute symptoms had subsided. A large number of these cases complained of burning at the meatus for some time after the injection. As the organisms disappear, the injections are gradually decreased, and when organism-free, M. was discontinued and copious irrigations of hot Kmno 4:10,000 were used, t. i. d. Patients were considered cured when several examinations showed negative urethral smears, clear urine (a few shreds are of no importance) negative prostate, vesicles, and no stricture formation present. In treating the cases of posterior urethritis, he used instillations of 1 per cent M. in a Keyes instillator, after a subsidence of the acute anterior symptoms. Prostate and vesicles were massaged, sounds passed, and urethra massaged after the pus had disappeared. In treating chronic gonorrhea, M. was used as an instillation every other day, and massage and dilatation used as indicated. Many of the chronic cases were of long duration, and organisms rarely found in the urethral smears.

Young (23). Reports very unsatisfactory results in the treatment of acute gonorrhea, but its use in chronic cases and in the declining stages of acute cases, after the use of other antiseptics for a week or ten days, has been most satisfactory. He reports one pyelitis case cured with two injections of 1 per cent into each pelvis and two very resistant chronic cases greatly improved but not cured.

Burns (24). Six cases of chronic colon bacillus cystitis were treated by the use of 1 per cent solution of M. Three of these were completely cured by two or three instillations with no reactions. The other three were improved but not cured, and two of these experienced marked reactions characterized by frequency and dysuria of several hours duration.

Robinson (25). Ten cases of acute anterior urethritis were cured in from four to ten days, and seven other cases with prostatic and seminal vesicle involvement of long-standing, one of four years, two of one and one-half years, two of one year, and two of six months duration—all showed marked improvement. Seven cases of chronic anterior gonorrheal urethritis of from one to four years duration were treated. Five were apparently cured in from one to four weeks, after they had resisted other treatment for a long period of time. Two cases were improved but not cured.

Estes (26). Reports a failure to render urine of any case of pyelitis culturally free from organisms. Cases improve up to a certain point, but do not become sterile. In bladder infections, especially the coccus infections, results are very striking, the urine becoming bacteria-free

in from ten to fourteen days. In acute gonorrhea, it is not so efficient as acriflavine or protargol, and its action in chronic gonorrhea is not especially striking.

Crowell (27). At the Crowell Urological Clinic some very brilliant results were obtained in cases of colon bacillus infection of the kidney pelvis and bladder by the use of M. locally. In infections due to other organisms the results have not been so gratifying. Better results were obtained in chronic infections than in the acute processes. Some very excellent results were obtained in Neisser infections and in some cases the results were not at all satisfactory. No case reports or details were given.

Kleiner (10). Kleiner reports 'excellent results in tubercular cystitis which had persisted for seven months following nephrectomy. A small ulcer of the bladder started to heal promptly when M. was used, and was entirely healed after twelve treatments. Also reports one case of severe cystitis associated with filiform stricture of the urethra. After dilatation of the stricture, cystitis was treated for one month with various antiseptics with no improvement. Four daily instillations of M. using 30 cc. of 1 per cent solution and allowing it to remain in the bladder, produced a complete and permanent cure in five days. A similar case of cystitis, due to residual urine from a large prostate, was completely and permanently cured by ten daily instillations of 1 per cent M. Four other cases of cystitis—one due to nerve injury, one to bilateral pyelitis, one to chronic seminal vesiculitis, and one due to contracted vesical neck—which had resisted prolonged treatment by other antiseptics, failed to show any improvement when treated by M. Thirty cases of acute and chronic gonorrheal urethritis were treated by the use of M., but the results were not superior to the results obtained by the use of other forms of treatment. In this series there occurred four cases of severe peri-urethral infection with edema of the whole penis, presumably due to the M. This edema subsided in from ten days to two weeks with hot applications and cessation of all local treatment.

Neel (28). Reports excellent results in many cases of vaginitis and endocervicitis. One case of acute specific vaginitis in a child of four years was rendered discharge and organism-free in six treatments, the details of which were not given.

Healy (16). Reports three cases of severe pyelitis of pregnancy (two of them bilateral colon infections) which responded promptly to lavage of the kidney pelvis with one-half of 1 per cent solution.

These cases had failed to respond to active treatment with urinary antiseptics by mouth, diet, rest, colon irrigations, etc.

A marked improvement in a case of resistant ulcer of vulva was obtained by the use of one-half of 1 per cent M. as a spray, frequently applied.

Wilder (29). Three cases of chronic colon bacillus bladder infection without kidney involvement were treated with M. Two cases were cured by four instillations. The other case was markedly improved by three instillations, but not cured at the time this report was sent in.

McComb (30). Reported fair results only with M-220 in gonorrhea; had not used the drug in other conditions.

Wynne (31). Two cases of chronic colon bacillus infection of the bladder were cured by the instillation of 0.5 M. into the bladder. One case required 7 instillations and the other 13. Another case of chronic colon bacillus infection of the bladder and kidney pelves with hydro-ureters and hydronephroses received instillations of 0.25 M. (into the bladder only) every six hours for three months with no improvement. All the cases reported in this series complained of severe burning and irritation following the introduction of M. into the bladder. No toxic symptoms were seen in any of these cases.

In non-gonorrheal leucorrhea as well as in chronic gonorrhea, the local use of 5 per cent M. has been very beneficial. Six cases of acute gonorrhea in the female have been cured by the local use of M. while it proved to be of absolutely no value in one other case. All cases reported in this series were in the female.

Randall (15). Reports three excellent results in old dispensary cases of stricture, with an almost immediate clearing up of infection and peaceful urination. These were chronic colon infections. M. is now used routinely after every passage of a sound. It is also used in all cases of prostatism under preparation for operation. No untoward results seen from its use. It proved irritating in one kidney pelvis. It is also used as deep instillation after prostatic massage.

It has not proved to be superior to other drugs in acute gonorrhea. There has been great deal of complaint about irritation, especially when sealed in the urethra. It has proved to be valuable in chronic anterior urethritis, especially when used with dilatations. In gonorrheal vaginitis in children good results are reported by its use as a tampon application.

It has been found to be of decided value in keeping wounds about

the genitalia sterile, such as operative wounds for cure of hypospadias and epispadias, where perfect sterility is essential for healing.

In a recent letter Randall states: "The general feeling about Mercurochrome-220 is concisely this: it is doing something that nothing else did before in the clearing up of chronic infections. We have not gotten uniform results. Sometimes miraculous, at others inert. Personally in these latter cases I feel that we have not, in all probability, properly studied the case and have not gotten the drug to the seat of the infection. It has found a place in our regular treatments to the exclusion of weaker antiseptics. I have succeeded in aborting five cases of acute gonorrheal urethritis when started within the first thirty-six hours after symptoms appeared (two were primary attacks). I have failed in others but feel so encouraged that it is always worth the trial. In urethroplastic work I have obtained splendid results, better than I have ever had before.

Snyder (32). Two cases of colon pyelitis cured by one or two pelvic lavages using M. Four cases of severe, long-standing, intractable cystitis, complicated by stone or malignancy improved and made comfortable but never rendered organism-free. As a result of his experience with M., he considers it the "most valuable urinary drug available." The alkali soluble form caused more burning than the solutions made from the sodium salt. Has not used the drug in acute urethral infections.

Hinman (33). Fourteen cases of chronic cystitis of colon bacillus type were treated with M., all with good results. He states that as a result of his experience with the antiseptic, he considers it one of the most valuable additions to urinary antisepsis. The results obtained in cases of chronic cystitis that sometimes persist after prostatectomy, following the use of M., have been most remarkable, infections sometimes completely clearing after two or three instillations, and if more are required, always being much improved. In chronic infections of the kidney pelvis, in acute and chronic gonorrhea, results have not been superior to those obtained by the use of other antiseptics in common use.

Stewart (34). "In the department of pediatrics Johns Hopkins Hospital a 1 per cent solution of M. has been used in two cases of gonorrheal ophthalmia and in one case of severe intractable pneumococcus conjunctivitis. These three cases cleared up more quickly than similar cases which in the past were treated with silver nitrate and argyrol. I might say that we always began treatment with one instillation of 1 per cent silver nitrate.

"Last year (1920) in our diphtheria service we had a great deal of difficulty for a time in discharging patients clinically well because of persistent positive nasal and throat cultures. In about twelve of these children, including the one with cleft palate, irrigations of the rhinopharynx with saline solution were followed by very careful and thorough painting of the rhinopharynx with 10 per cent M. Most of the cultures taken three succeeding days were negative. A few remained positive and the treatment was repeated, this time using 20 per cent M. with successful results. The same practice has been followed this year with the children who continued to have positive cultures after recovery. We have failed to obtain negative cultures after this treatment in only two or three instances and since then these children have become negative and all have been discharged. This is a much better record than before the adoption of this treatment. I would hesitate to say at this stage, *i.e.*, after the treatment of only about twenty-five children, that mercurochrome is invariably effective in treating diphtheria carriers, but it certainly has proved so far to be the most effective treatment that we have been able to find."

Leonard (35). "I have used Mercurochrome in cases of contracted bladder and infection of colon bacillus, with very beneficial results. The use of M. cleared the infection entirely. I also used irrigations of 0.25 per cent for 12 treatments. I have several cases of severe cystitis with alkaline urine and large quantity of pus following operation for stricture, external urethrotomy. Three of the cases I have in mind now, the severe bladder condition has existed for a period of over two to four years. They also had irrigations of Mercurochrome and responded very nicely after treatment of several months. I have used it in four cases of posterior urethritis associated with chronic prostatitis and have used irrigations of Mercurochrome from 0.5 per cent to 1 per cent and it has been very helpful in connection with the ordinary systematic massages."

Tankersley (36). "I have used Mercurochrome 1 per cent solution irrigations of the pelvis, of the kidney and bladder several hundred times during the last six to eight months, and I find it the most satisfactory antiseptic for this class of work of any of the solutions. In addition to this, my work being general surgery, I have used it for practically everything where iodine in any strength could be used. I have had some splendid results when injected between fragments of bones in compound and comminuted fractures, especially in badly infected cases. I have used it to wash out appendicial abscess where

walled off. Recently, in a ruptured ulcer of the stomach, after about eight days I injected a weak solution through the drainage tube down to the seat of the rupture, and drainage practically ceased in three days. I am using it now as a routine in painting over all wounds, clean or infected, and especially contused and lacerated tissues due to accidents, and I must say I get better results than in like treatment with iodine. I am very much pleased with this solution and wish to congratulate you on giving us such a splendid non-irritating antiseptic. I am swearing by it but the hospital authorities are swearing at it. The stain is the only bad feature, something that I do not personally object to."

Clapp (37). "Replying to your inquiry as to clinical experiences in eye cases where M. was used, I desire to say that continued use in gonorrheal ophthalmia has confirmed my opinion as expressed in the article on 'Use of M. as a germicide in ophthalmia-neonatorum,' J. A. M. A., May 1, 1920."

If used early and at short intervals (two hours) and in a strength of not less than 2 per cent, it certainly causes a disappearance of the organisms and lessening of the pus more rapidly than any of the antiseptics we have used. It has also seemed to arrest ulcers of the cornea secondary to infected conjunctiva and restore the healing process very satisfactorily.

Owing to the disagreeable staining, it is not a preparation that lends itself to treatment of the minor cases of conjunctivitis, but in all the more severe forms of infection and especially so in the gonorrheal types it is a very valuable addition to our armamentarium."

Roberts (11). "I have used Mercurochrome in 0.25 per cent solution in cases of seminal vesiculitis after vasotomy with good results. In fact, I had one case of several months' duration in which only one of the vesicles was injected, resulting in a cure. In another case I put 10 cc. of Mercurochrome-220 solution in each side in two weeks after which he had a nocturnal emission containing so much of the medicine that he thought he had a hemorrhage. These cases were chronic and of long standing. The results were very gratifying and gave promise of proving Mercurochrome-220 to be another good drug to use in these cases."

Crowe (38). "We have used M. in the oto-laryngological department of the Johns Hopkins Hospital during the past year with the most gratifying results. In 5 and 10 per cent solution it is not toxic, is not irritating, and on account of its penetrating properties is especially

suitable as a bactericidal agent in acute and chronic infections of the mucous membrane lymph-adenoid tissue of the nose, throat, larynx and middle ear. In our experience M. as a local application has been more efficacious and less irritating than silver nitrate solutions, argyrol, methylene blue, gentian violet or any of the phenol preparations.

"The following are some of the conditions in which we have used M. to great advantage:

"1. In acute coryza or acute pharyngitis the application of a 10 per cent solution to the mucous membrane of the nose, naso-pharynx and pharynx will abort the attack if applied within the first 12 hours after the onset of symptoms. The mucus is first removed with an alkaline spray or swab and the drug then applied on a cotton swab will penetrate to the submucosa and have an inhibiting influence on the organisms in the crypts and glandular elements of the mucosa. We know of no other drug that will do this with so little irritation.

"2. Acute and chronic maxillary sinus infections afford the best opportunity for studying the toxicity, irritating properties and bacteriocidal effects of M. In all antrum infections the mucous and pus should be first removed by irrigation with a normal saline solution, the sinus filled with the M. solution and the trochar withdrawn. In the chronic cases a 5 per cent solution should be used; in acute infections a 1 per cent solution. We have never seen any toxic symptoms in any of our series of about 150 cases.

"3. In the post-operative treatment of mastoid and ethmoidal cavities M. is preferable to Dakin's solution because it does not kill the young granulation tissue.

"4. In some cases of chronic suppurative otitis media M. applied to the nasal-pharynx, Eustachian tube and middle ear will result in a rapid cessation of the discharge. We have used a 5 per cent solution in the ear in a series of about 20 children and 50 adults with no untoward symptoms in any cases.

"If carefully and thoroughly applied, a 20 per cent solution will probably prove to be a valuable agent in the treatment of ozena, Vincent's angina and chronic diphtheria carriers. The main objection to the use of Mercurochrome is the inconvenience caused by the staining of the skin around the nose after the application in the nasal cavities. This can be prevented to a certain degree by the liberal use of cold cream."

Bidgood (39). "In the Hunterian Laboratory infected wounds in dogs have usually been treated by irrigations of boric acid solution,

dichloramin-T in oil, or with pure carbolic and alcohol. Dakin's solution has also been used, but the technique is difficult in dogs and often no treatment has been given. We have recently used M. in 2 to 5 per cent solutions, once daily, with more rapid sterilization and healing than with any previous method. The simplicity of technique commends it."

Cumming (12). The following interesting case is furnished by Dr. R. E. Cumming, Chief, Section of Urology, Walter Reed U. S. A. General Hospital, Washington, D. C.

Venereal history: Neisser infection in 1916. Was treated for one month and pronounced cured.

Army history: Enlisted in November 1917, and served overseas with infantry.

Present medical history: In May, 1919, while on duty in France, was bothered by general weakness. This condition grew gradually worse with no other symptoms and no apparent cause until July, 1919, when his urine began to be bloody and urination became painful. He was admitted to a hospital in France on July 6, 1919, with the diagnosis of cystitis, acute, hemorrhagic, cause unknown. Symptoms comprised dysuria, hematuria and extreme frequency, small quantities of urine, constantly bloody. He was kept in bed and improved with treatment consisting of urotropin and bladder irrigations three times a day with weak permanganate solution. By the middle of August, 1919, at which time he was evacuated to the United States, the bladder had improved a great deal and the hematuria had ceased. He was kept for ten days at Camp Merritt, New Jersey, and transferred to Walter Reed Hospital about September 1, 1919. His condition was again more severe with marked symptoms, such as noted above. Bladder urine cultures showed pure colon bacillus infection. He was treated with irrigations as follows: Weak permanganate, twice daily, and on the following days argyrol solution twice daily—the treatment used on alternate days. Early in September, 1919, a cystoscopy revealed a severe cystitis, involving the entire bladder mucous membrane and extending well into the sphincteric region, with areas of bulbous edema and a great amount of peeling mucosa. The following diagnosis was made: Cystitis, chronic, due infection with colon bacillus; Paracystitis, chronic. Repeated cultures revealed no organisms other than those noted. No evidence of tuberculosis could be found although at the time of recorded cystoscopy the ureters were not catheterized. After the patient had shown some improvement and was

able to be up and about, the irrigations were given more frequently, the treatments alternating the use of black silver salts, potassium permanganate, and solutions of silver nitrate. In November, 1919, it was determined to discharge the patient on S. C. D. as it was thought he had reached maximum improvement. He was cystoscoped again and the bladder showed very little improvement in appearance although the patient was patently very much better. The ureters were catheterized with difficulty and urine collected from each kidney. Both specimens were cloudy and contained an abundance of organisms as proved by smear and culture. The additional diagnosis was made: Pyelitis, bilateral, chronic, infection due colon bacillus, ascending type. The kidney pelves were lavaged at this examination with 1 per cent silver nitrate. Bladder treatment was then continued. In addition to irrigations, dietetic treatment was used and the intermittent use of urotropin. During the first week in December, 1919, the patient developed acute pain in left side, in the region of kidney. He was transferred to a ward as a bed patient and urine showed the findings constant at other times, albumen, pus and some blood cells. A cystoscopy demonstrated the fact that the bladder condition was getting more severe again. Separate kidney urines again cultured colon bacillus and showed a more massive infection on the left side. Combining bed care with daily irrigations and pelvic lavage at the time of cystoscopy just mentioned, the evidence of acute pyelitis disappeared in one week. It was then determined to use M. in an attempt to improve the pyelitis and cystitis.

The history of this case is given in some detail in order to show the exact condition of this individual patient, and the problem presented for a new agent in treatment. (See table on page 374.)

Cumming also reports the following: "Since the completion of this report, some fifteen cases have been added to the series with an even higher proportion of good results; we are now using M. as a routine for vas injection.

"You will be interested to know that we have been using Mercurochrome-220 almost exclusively for gonorrhea since the last report you had from us, and that the results have been highly satisfactory."

Treatment with Mercurochrome

TREAT- MENT	DATE	VOIDED URINE	RESIDUAL	URETERAL CATHETERI- ZATION	CULTURE	PRELIMINARY IRRIGATION	BLAD- DER CAPAC- ITY	TIME M. RETAINED	IRR- IGATION	FREQUENCY	PER CENT SOLU- TION	PER AMOUNT
	1919		cc.				cc.					
1st	Dec. 16	Cloudy	20	Both cloudy	B. coli, bladder and both ure- teral	Hot saline	100	5 min.	None	Severe	1	30
2nd	Dec. 18	Cloudy	30			Hot saline	170	10 min.	None	Less se- vere	1	60
3rd	Dec. 20	Cloudy	None			Same	200	45 min.	None	Less se- vere	1	90
4th	Dec. 22	Cloudy	None			Same	200	1 hour	None	Less se- vere	1	90
5th	Dec. 31 1920	Cloudy	None			Same	200	1 hour	None	Still less	1	90
6th	Jan. 2	Cloudy	25			Same	180	1 hour	None	Still less	1	90
7th	Jan. 4	Cloudy	None			Same	200	1 hour	None	Same	1	90
8th	Jan. 6	Less cloudy	None			Same	225	1 hour	None	Same	1	90
9th	Jan. 8	Less cloudy	None			Same	230	1 hour	None	Same	1	90
10th	Jan. 10	Less cloudy	None	Both clear	Bladder sterile	Same	245	1 hour	None	Same	1	90
11th	Jan. 12	Clear	None		Both ureters sterile	Same	260	1 hour	None	Same	1	90
12th	Jan. 14	Clear	None			Same	275	1 hour	None	Same	1	90
13th	Jan. 16	Clear	None			Same	300	1 hour	None	None	1	90
14th	Jan. 18	Clear	None			Same	375	1 hour	None	None	1	90
15th	Jan. 20	Clear	None			Same	375	1 hour	None	None	1	90
16th	Jan. 22	Clear	None		Bladder sterile	Same	200	1 hour	None	None	1	90
							300	1 hour	None	None	1	90

Examination of the accompanying table shows a remarkable improvement in the case after a series of only 16 treatments. The fact that the preparation causes no irritation is tremendously in its favor.

N. B.: The data on this case were submitted in a report, of which this is a copy, to the Surgeon General of the Army early in 1920. Robt. E. Cumming, Lt. M. C., Chief, Section of Urology.
July 14, 1920. Urine remains sterile.

SOME SPECIAL CASES TREATED BY MERCUROCHROME GIVEN IN
BRIEF DETAIL

Case I. Pyelitis, bilateral (colon bacillus). Sterilized by 12 treatments.

No. 8507 B. U. I., February 10, 1920, D. M. H., fifty-eight married.

Diagnosis: Pyelitis, cystitis, prostatitis.

Complaint: Loss of semen.

Genito-urinary history, negative.

Present illness: Began twelve years ago with loss of seminal fluid. Lately, difficult intercourse due to premature ejaculations; also inability to empty urethra at the end of urination. No pain or dysuria or frequency.

Examination of urine: slightly cloudy in three glasses with shreds and micro bacilli.

Genitalia: Negative. Rectal, prostate slightly indurated. Left seminal vesicle slightly indurated along outer edge. Right seminal vesicle soft, slightly adherent. On cystoscopy, no residual urine. Small translucent cysts on vesical orifice; otherwise negative. Both ureters catheterized, right with some difficulty. Specimens examined show a bilateral colon bacillus infection; phthalein 15 per cent on each side in thirty minutes. Prostatic secretion contained pus cells and bacilli. Two pelvic lavages with mercurochrome cleared up the pyelitis; bladder urine, however, remained infected until after twelve treatments, once daily with irrigation of sterile water, followed by mercurochrome instillation and occasional prostatic massage, when it becomes free from infection and remained free.

Case II. Pyelitis, bilateral; cystitis. Sterilized by 4 and 8 treatments respectively.

No. 8003 B. U. I., September 3, 1919. E. S. B., forty nine.

Complaint: Patient complains of left swollen testicle.

Past history: Frequent attacks of rheumatic fever. Had St. Vitus' dance and is very nervous; subject to headaches and dizzy spells.

Genito-urinary: No venereal disease. Some hesitancy and dysuria in the past. Sexual power markedly diminished. Twelve years ago a course of prostatic massage.

Present illness: Began suddenly a few days ago with an acute epididymitis; since then patient had frequency and dysuria and hesitancy.

Genitalia: Negative, except swollen left epididymis and slight hydrocele on both sides. Prostate and seminal vesicles indurated.

Examination of urine: Cloudy and microscopical examination shows bacilli and pus. August 21, fourteen days later, ureters catheterized; specimens from both sides show pus cells and bacilli. Phthalein 25 per cent on each side in thirty minutes. September 1, patient's ureters catheterized and 1 per cent AgNO_3 injected, followed by reaction and pain.

September 3 mercurochrome was used for pelvic lavage, no reaction. Four pelvic lavages with mercurochrome given every other day cured the pyelitis. After a further course of prostatic massage and KMnO_4 irrigations and four instillations of mercurochrome, patient became free from infection and urine macroscopically clear, the symptoms began to disappear and his condition markedly improved. On October 31 was discharged as cured, urine free from infection and symptoms having all disappeared.

Case III. Pyelitis, double. Sterilized by 13 treatments.

No. 8171 B. U. I., October 3, 1919. W. A. S., fifty-one, married.

Complaint: Discharge, dysuria, pain in back, painful ejaculation.

Genito-urinary: No venereal infection; hematuria four years ago, duration four days. Fourteen months ago second attack of hematuria, duration one week. Treated for prostatic trouble during the past two and a half years. Seven weeks ago swelling of left testicle appeared.

Present illness: Began one month ago with a discharge and burning on urination and frequency during the day; also painful ejaculation and pain in the back.

Examination of urine: Cloudy in three glasses. Microscopically, showed large amount of pus and many large bacilli.

Genitalia: Urethral discharge contains pus and large bacilli. Prostate and seminal vesicles indurated. Prostatic secretion showed very large amount of pus. Cystoscopy shows a reddened trigone, injected ureteral openings and a small diverticulum in left lateral wall of bladder. Ureters catheterized and specimens from both kidneys show pus and bacilli.

After three treatments with mercurochrome, the pyelitis cleared up and no recurrence followed until November 11 when catheterization of ureters again showed infection of both kidneys. One treatment with mercurochrome 1 per cent promptly cleared up the infection of the bladder urine. On December 6 recurrence followed and mer-

eurochrome promptly cleared the infection, ten treatments being required (daily instillations). Patient left December 16 with urine clear and uninfected, feeling fine and symptoms almost entirely gone. Prostatic secretion still showed pus but was markedly improved.

On January 7 patient returned for examination. Kidneys were free from infection and patient says he has improved remarkably.

Case IV. Prostatic bar, chronic cystitis; punch operation. Sterilized by mercurochrome.

No. 8425 B. U. I., J. M. J., thirty-one, married.

Complaint: Difficulty in urinating, strong odor to urine.

Genito-urinary: Ruptured urethra in 1909, perineal and suprapubic operation; incontinence for one year. Marked frequency and urgency for two years; then improved until 1915; developed Neisser infection, frequency and urgency returned, and stream began to diminish in size. Treated for three years with sounds. In April, 1919, began to notice strong odor to his urine.

Examination: Marked prostatitis and vesiculitis. On cystoscopy 100 cc.; chronic cystitis and prostatic median bar. Colon bacillus infection of urine; marked odor and very cloudy. In spite of obstruction, after ten daily treatments with mercurochrome, 1 per cent urine became clear and free from infection.

January 20, punch operation; satisfactory convalescence. January 26 urine cloudy and infected (colon bacillus). Three daily treatments with 1 per cent mercurochrome freed urine from infection. Three days later a few bacilli were again found in urine and treatment was given as before. Next day it was free from infection and there was no recurrence; under observation ten days. Patient discharged as cured and feeling well and with no symptoms.

Case V. Prostatitis, chronic posterior urethritis. Urine sterilized in 6 treatments.

No. 8597 B. U. I., March 18, 1920. M. F., thirty-four, married.

Complaint: Pain in coccyx and perineum.

Genito-urinary: Negative.

Present illness: Began two years ago over right kidney, followed immediately by cloudy urine and marked frequency and dysuria. A course of prostatic massage and irrigations improved his condition but in July of last year his symptoms became more aggravated. He has had various sorts of treatment without results. At present he has dysuria, a soreness in perineum and a weak back.

Genitalia: Prostate larger than normal, slightly indurated and adherent. Seminal vesicles negative. Prostatic secretion negative.

Urine: Bacilli, cocci and a few pus cells.

After six treatments with irrigations and instillations of 1 per cent mercurochrome and prostatic massage, the urine became negative, his backache disappeared. Patient noticed marked improvement in his condition after seventeen days of treatment and examination showed no recurrence of infection. The patient was treated by massages and irrigations of KMnO_4 at intervals for six months. No return of infection during that time.

Case VI. Interstitial cystitis; bacillary. Sterilized in five days.

No. 8470 B. U. I., January 21, 1920. Mrs. W. T. P.

Past history: Tuberculosis on mother's side of family.

Present illness: Three years ago patient noticed marked frequency both day and night; for past year marked frequency, dysuria and hesitancy.

Urine: Examination showed chronic cystitis; bladder capacity 175 cc., cloudy, containing pus and bacilli.

January 21, after five days treatment with mercurochrome instillations, patient greatly improved but urine was still infected. January 30: Patient has greatly improved; holds her urine two to three hours without discomfort. Urine is grossly clear and microscopically free from infection. February 20: Patient has improved markedly under instillations of mercurochrome, and dilatations. Voids two or three times at night and every three hours during the day. Patient's greatest improvement has been in the disappearance of pain and frequency. March 1: Patient is leaving for home. Under instillations of mercurochrome and irrigations she has greatly improved. Intervals of urination have increased from one-half to three and four hour intervals, and pain has almost entirely disappeared. Bladder urine is quite clear and free from infection.

Case VII. Chronic gonorrheal urethritis. Sterilized in 6 treatments.

No. 8363 B. U. I., December 2, 1919. G. H. S., twenty-two, single.

Complaint: Discharge from urethra.

Genito-urinary: Negative.

Present illness: Began one week ago, two days after exposure, with burning on urination and followed by a discharge. No other symptom.

Examination: Watery urethral discharge containing extra-cellular diplococcus bacilli but no intra-cellular organisms.

Genitalia: Negative. Prostate indurated and markedly abnormal. Seminal vesicles indurated. After three days, twice daily treatment with anterior irrigations of sterile water and injections of Mercurochrome into anterior urethra, the organisms disappeared and there was no recurrence after two weeks. After the third day there was marked irritation of the urethra. Mercurochrome was discontinued and anterior KMNO_4 irrigation was given for seven days. On December 20th patient was still free from infection and there were no symptoms except a slight watery discharge.

Case VIII. Posterior urethritis and prostatitis. Sterilized in 19 treatments. No. 8166 B. U. I., October 1, 1919. E. D. G., forty-four, single.

Complaint: Frequency and burning on urination.

Genito-urinary: Negative.

Present illness: Began three years ago with sharp pain at end of penis, he soon developing some difficulty on urination. At that time diplococci were found in his urine; treatment gave no relief. About one year ago began to develop marked frequency, it being necessary to get up five to seven times at night to urinate. At present time patient has frequency, dysuria and some dribbling, although he has been treated by six different doctors.

Genitalia: Small area of induration in left prostatic lobe. Prostatic secretion contained pus cells and short bacilli.

Urine: Few pus cells and many short bacilli and few cocci. After five days' treatment with irrigations of KMNO_4 and injections of Mercurochrome twice daily, and three days' treatment by irrigations of sterile water followed by injections of 1 per cent Mercurochrome three times daily, patient's urine became free from infection, and during seven days observation there was no recurrence, and patient was permitted to return home on October 17. Symptoms had disappeared except for a slight irritation at the end of the penis.

Remark: Injections were given here instead of instillations. Anterior urethritis was produced which immediately cleared after cessation of the drug.

Case IX. Chronic prostatitis, chronic seminal vesiculitis, prostatic hypertrophy, median bar. Coccus infection. Sterilized in 8 treatments.

No. 5165 B. U. I., March 4, 1920. G. A. R., fifty-one, married.

Complaint: Frequency, chills and fever (intermittent).

Genito-urinary: Negative.

Present illness: Began six years ago with frequency of urination accompanied by chills and fever. These attacks have recurred about twice a year until past eight months when these attacks became more frequent. Since December had three severe attacks of frequency, chills and fever, but no other urinary symptoms except dysuria during the attacks.

March 26, urine: shreds in first specimen, second and third clear but containing pus cells and cocco. Ureter catheterization shows both kidneys free from pus and bacteria. Rectal examination reveals a prostatitis. Prostatic secretion contains pus cells and cocci.

After three treatments (prostatic massage followed by irrigations and instillations of Mercurochrome), the prostatic secretion and urine became free from infection and remained free for three days when examination again showed cocci and bacilli in urine and cocci in prostatic secretion. Two more treatments cleared up this infection and patient remained free from infection.

April 8, patient feels perfectly well, urine is clear in three glasses, no shreds, no infection. Symptoms have completely disappeared.

April 10, patient says he feels well. Is permitted to go home.

Case X. Chronic prostatitis, urinary infection. Sterilized by one treatment.

No. 8511 B. U. I., February 13, 1920. H. E. S., thirty-nine, married. Complaint: Abscess of prostate and colon bacillus infection.

Genito-urinary: Neisser infection at age of twenty-six; duration three weeks, with left sided epididymitis. Impaired sexual powers for past three years.

Present illness: Began five years ago with dysuria, soon followed by frequency, dribbling and nervousness. Two weeks ago consulted a doctor "who found colon bacillus in urine." Following prostatic massage, patient says he developed a prostatic abscess and the doctor sent him to a hospital for operation. Instead, he immediately came here for treatment.

Examination: Patient is in a wheel-chair and markedly depressed. Left epididymis indurated. Rectal examination very painful, slightly indurated; slightly adherent prostate.

Urine: Few shreds in first glass, second and third glass slightly hazy. Microscopically, few pus cells, many cocci, no bacilli. One treatment by massage of prostate with irrigation and instillation of Mercurochrome cleared the urine of infection and three treatments removed the pus. From February 14 to March 20 no recurrence of infection.

Patient discharged. "He feels well and all his symptoms have disappeared."

Case XI. Chronic prostatitis, cystitis, iritis. Sterilized in six treatments, recurred after forty days; again sterilized in six treatments; no recurrence since.

No. 8499 B. U. I., February 5, 1920. C. C. G., forty-nine, married.

Complaint: Frequency, some pain over the bladder, prostatic trouble and iritis.

Personal history: Iritis for past ten years.

Genito-urinary: Neisser infection at twenty-one and again at twenty-three and twenty-five years of age.

Present illness: Began last September with a severe attack of iritis. In December developed frequent nocturnal emissions, weakness and nervousness, later followed with frequency of urination (three to six times at night) and pain at the neck of bladder followed by dysuria and occasionally dribbling.

Genitalia: Negative. Prostate indurated. Right seminal vesicle negative. Left seminal vesicle enlarged and indurated.

February 5, urine clear except for large shreds in three glasses. Prostatic secretion contained pus and short bacilli. Urine cloudy and infected with short bacilli.

After six treatments, twice daily with irrigations of sterile water and instillations of Mercurochrome, with massage of the prostate, patient's urine became clear and uninfected and prostatic secretion became sterile. From February 13 to March 5 there was recurrence of infection. Soon after treatment was begun, patient noticed that his eye trouble began to improve; he was able to read and discarded his heavy smoked glasses for a lighter pair. He felt that the treatment had been the cause for this improvement, as treatment of the eyes had never produced such marked improvement. By February 17 the patient felt that marked improvement had taken place in his entire condition and that his symptoms had practically all disappeared. On March 5 he was permitted to go home, seemingly in perfect condition. On March 25 patient returned complaining of frequency and nervousness at night but not during the day. Examinations of urine showed it to be clear, few shreds in first glass, third glass few pus cells and bacilli, and the prostatic secretion showed pus cells. After treatments twice daily with irrigations of sterile water followed by Mercurochrome, instillation and prostatic massages on alternate days, patient again improved and became free from infection. On April 6 he says he feels

quite well. Rectal examination showed a marked improvement of prostate and seminal vesicles. Eye condition apparently cured. On April 10 patient permitted to go home; free from symptoms and infection.

Case XII. Stricture of urethra, infection from instrumentation. Sterilized in 10 treatments; recurrence of infection fourteen days later.

No. 8484 B. U. I., January 24, 1920. D. C. S., sixty-nine, single.

Complaint: Frequency, prostatic trouble and stricture.

Genito-urinary: Neisser infection at thirty; duration three weeks. Second Neisser infection at thirty-two; duration six months, no complications. For past five years has had to get up three or four times at night to urinate. Irritation in deep urethra and head of penis. Occasionally some dysuria.

Urine: Clear, no infection. Stricture at bulbo-membranous junction. Sound 16F passed without difficulty. Prostate indurated. Prostatic secretion: many pus cells, no organisms. Stricture dilated without difficulty. On January 29 30F sound was passed.

January 30, cystoscopy: Residual urine 75 cc.; anterior prostatic bar; bladder trabeculated; many small calculi present. February 10, catheterized specimen slightly cloudy. Microscopic examination of urine showed few pus cells, many cocci. Prostatic secretion also infected with cocci. Daily treatments with irrigations of sterile water and instillations of Mercurochrome and stanoxyl tablets by mouth; After 10 days the urine became clear and free from infection. Prostatic secretion also free from infection after five prostatic massages. Subsequently observed for five days with no recurrence. Two weeks later patient returned for examination and urine contained cocci but the prostatic secretion was free from infection. He could not remain for treatment but is to return later.

Case XIII. Seminal vesiculitis; cocci and bacilli present. Sterilized by 5 treatments.

No. 7444 B. U. I., April 1, 1920. R. B. M., fifty-eight., widower.

Complaint: Burning in region of neck of bladder at the end of urination for past two months, and at times slight terminal hematuria. Frequency every hour during day, four to five times at night. Three weeks ago developed pain in the back and hips and tenderness in his testicles.

Genito-urinary: Neisser infection at seventeen. Left epididymitis. Second attack at twenty-five. Bilateral epididymitis. Bladder trouble in January of 1919.

Examination: The right vas was tender and indurated; both epididymes indurated. On rectal examination, prostate was small, flat and soft; vesicles hard and nodular.

No infection of the urine but prostatic secretion contained a few pus cells, cocci and bacilli. After five treatments with prostatic massage followed by irrigations of sterile water and Mercurochrome 1 per cent instillations, patient noticed marked improvement and was found to be free from infection.

April 14, patient's urine is clear and prostatic secretion has remained free from organisms and symptoms have entirely disappeared.

Case XIV. Stricture of urethra with infected urine. Sterilized in 10 treatments.

No. 8640 B. U. I., March 26, 1920. M. F. seventy, married.

Complaint: Frequency and burning on urination.

Genito-urinary: Admits Neisser infection; does not remember how many attacks or duration. Has had severe complications with attacks. No other history.

Present illness: Began four years ago with frequency of urination. One year ago developed dysuria and dribbling, hesitancy, difficulty and diminution in size and force of stream. Nocturnal urination now eight to ten times.

Examination: Penis negative except for a small meatus. Both testicles small; both epididymes indurated and nodular. Rectal examination shows an indurated nodule in left lobe of prostate; otherwise negative. Bougie a boule met obstruction about $\frac{3}{4}$ inch behind meatus. Filiform passed through stricture into bladder. Dilated to 24F with followers. Urine: cloudy with pus and bacilli.

After ten treatments once daily with irrigations of sterile water, followed by injections of Mercurochrome 1 per cent, patient's urine became clear and uninfected, and his symptoms began to disappear. Stricture was also dilated to 28F.

April 15, urine clear; no infection, no symptoms except that patient gets up once or twice at night to urinate.

Case XV. Chronic cystitis; colon bacillus. Sterilized by 10 treatments.

No. 1489 B. U. I., September 19, 1919. A. F. F., forty-two, married.

Complaint: Frequency, dysuria and pain in groin.

Genito-urinary: Neisser infection at age of seventeen. In 1903 had prostatitis. In 1908 treated here for prostatitis, vesiculitis and colliculitis. Treated off and on for three years. September 19, 1919,

patient returned complaining of frequency and dysuria, and pain in groin. Urine cloudy and contains bacilli. Culture shows colon bacillus.

Patient was given sterile water irrigations and instillations of 1 per cent Mercurochrome twice daily. After ten treatments patient's urine became clear and free from organisms; his symptoms almost entirely disappeared except pain on ejaculation, and patient himself felt markedly improved. Samples of urine and prostatic secretion examined in October, November and December showed no infection.

Case XVI. Right pyelitis; colon bacilli. Sterilized by 15 treatments.

No. 8850 B. U. I., June 11, 1920. Mrs. L. S. S., forty-five., married.

Complaint: Attacks of pain in right side of back, with chills and fever.

Family history: Father died of kidney trouble. Mother died of pulmonary tuberculosis. Grandfather and several uncles and aunts had kidney trouble.

Present illness: Patient was in good health until present illness. Present illness began about two years ago with sudden onset of frequency, every half hour during the day and three to six times during the night; urgency, dribbling and violent headaches. Acute attack lasted about one week but patient has never been free from symptoms since. For past six months she has also been having attacks of sharp pain in the right upper abdomen and back. This pain does not radiate and does not seem to have any effect on her urinary symptoms.

Examination: Bladder urine shows pus and large bacilli. On cystoscopy, bladder mucosa not injected. Both ureters catheterized with ease and a specimen collected from both kidneys. Specimen from left kidney was normal; from the right showed a moderate amount of pus and a moderate number of large bacilli. X-ray of kidneys negative.

Patient received nine treatments by lavage of the right kidney pelvis with 1 per cent Mercurochrome and six treatments by lavage with AgNO_3 1 per cent. She was then free from infection and relieved from her symptoms. Patient was seen six weeks later and was still free from infection and from symptoms.

Case XVII. Stricture of urethra; urethral chills following dilatation. Aferward apparently prevented by injections of 1 per cent Mercurochrome.

No. 9010 B. U. I., August 17, 1920. G. F. thirty-two., married.

Complaint: Difficult urination.

Genito-urinary: Gonorrhea nine and two years ago; duration unknown. About two years ago noticed diminution in size and force of

urinary stream. No previous treatment. Attempts to pass filiforms were unsuccessful. Small whale-bone bougie was passed through the stricture and tied in place. This was followed by a chill and high temperature. On the following day filiforms and followers were passed. This was again followed by a chill and a temperature of 104.5°. After subsequent instrumentations, an instillation of 1 per cent Mercurochrome was made and no reaction followed.

Tabulations of clinical experiences with mercurochrome

Urethritis

Cases of acute urethritis treated with M	187
Cases tabulated.....	100
Cases not tabulated because details were lacking, but in which satisfactory results were obtained.....	87
Of the tabulated cases:	
Number followed until apparently cured.....	32
Number discontinuing treatment.....	68
Shortest time required to render the urethral discharge free from orisms.....	4.0 days
Longest time required (a) by injection.....	36.0 days
Longest time required (b) by irrigations.....	84.0 days
Average time required.....	16.8 days
Number with anterior involvement alone.....	61 per cent
Number with anterior and posterior urethral involvement.....	39 per cent
Number developing complications after starting treatment.....	7 per cent
These cases are all public dispensary cases and many of them negroes.	

Cystitis

Number of cases tabulated.....	40
Number of cases cured.....	30 to 75.0 per cent
Number of cases improved.....	7 to 17.5 per cent
Number of cases not improved.....	3 to 7.5 per cent
Smallest number of treatments needed to render urine free from organisms..	1
Smallest number of days under treatment.....	1
Largest number of treatments needed to render urine free from organisms..	23.0
Largest number of days under treatment.....	60.0
Average number of days under treatment.....	18.5
Average number of treatments.....	7.6

Pyelitis

Number of cases tabulated.....	17.0
Number of cases cured.....	10 to 58.0 per cent
Number of cases improved.....	4 to 23.2 per cent
Number of cases not improved.....	3 to 17.4 per cent
Average number of pelvic lavages given cases cured.....	9.2
Smallest number of treatments needed.....	3.0
Largest number of treatments needed.....	12.0

CONCLUSIONS

1. Mercurochrome is an effective germicide but has not proved to be vastly superior to all other drugs in acute gonorrhea, although certainly quite efficient. The intense stain is a drawback to its use as an injection by the patient. Acriflavine is free from this objection.

2. In chronic infections of the urethra, prostate and vesicles its great value has been amply proven. It penetrates deeply and may be found in the prostatic secretion several days after posterior instillation.

3. The results obtained in many cases of chronic cystitis are remarkable, long standing infections often clearing up in a few treatments. The coccus infections are more resistant to Mercurochrome than the colon bacillus infections. In some cases which fail to become sterile, constant reinfection of the bladder is found to occur from kidneys or prostate.

4. Mercurochrome is less irritating and produces less reaction in the renal pelvis than silver nitrate solution, while possessing about equal germicidal powers, but in some cases both drugs should be used alternately and sometimes silver is better.

5. In some cases of pyelitis, the infection comes from teeth, tonsils, etc. and sterilization of the pelvis is impossible until the primary focus is cured.

6. Continued use has proven Mercurochrome to be a most satisfactory dressing for venereal ulcerations and buboes.

7. In general surgery, reports indicate that Mercurochrome is very valuable in dressing open wounds and sinuses.

8. The germicidal efficiency of the drug in other branches of medicine and surgery has been proven, especially in the treatment of infections of the throat, nose, sinuses, ear and eye. It is reported to be most efficient in disinfecting the throats of diphtheria carriers. This alone makes Mercurochrome an addition to therapeutics of great value.

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FLUOROSCOPIC EXAMINATION OF THE INJECTED KIDNEYS, AND REPORT OF A CASE¹

F. R. HAGNER

Fluoroscopic examination of the kidneys, both with and without injection of the pelvis of the kidneys, is, I believe, a valuable adjunct to the accurate diagnosis of certain kidney conditions. It can often be definitely settled whether a shadow in the kidney region is caused by a calculus in the kidney or is due to some calcareous deposit in the gland or some other organ. The X-ray catheter or injection of the pelvis may be necessary to make an accurate diagnosis, the fact of being able to see the catheter in place and observing the simultaneous movement of the catheter and the shadow of the calculus caused by the respiration will often help materially in clearing up the diagnosis. Our ability to see the kidney injected and to watch the fluid escaping into the pelvis often gives us information more valuable than roentgenography.

I will quote Dr. Merritt, the roentgenologist of Garfield Hospital, who summarizes his views and gives his technique, as follows: The method assists materially in locating the kidney and estimating its size. Stereoscopic plates are always made afterwards as a matter of record but they seldom if ever give additional information and many times the lesions show more plainly in the fluoroscopic than in the X-ray plates.

The essential points are as follows:

1. A low gap, not more than four inches and as low as two.
2. Five milliamperes of current.
3. Absolutely darkened room, with operator protected from daylight at least twenty-five minutes prior to the examination.
4. The patient having been previously catheterized, is brought in on an ordinary hospital cart and transferred to the X-ray

¹Read at the meeting of the American Association of Genito Urinary Surgeons, Rochester, Minn., May, 1920.

table when the injection of the ureters may be performed at the pleasure of the urologist.

I have an interesting observation to report but will not go into the history of the case except briefly. This was a case of pyelitis in which we made a diagnosis of a suppurative perinephritis.

Both Dr. Fuller and I thought there was possibly some connection between the pelvis of the kidney and the suppurative process outside the kidney. Patient's kidney was injected and fluoroscopic examination was made during injection of the kidney. As soon as 10 cc. of thorium was injected into the pelvis, the injected fluid began to escape into a cavity outside of the nephritic tissue. Another 10 cc. was injected and the fluid could be seen escaping out into this cavity in a stream—no force being used—patient complaining of no pain. This showed much more distinctly while watching it than it does in the plate I have here.

At operation the next day, when the kidney was exposed and the abscess cavity explored it was found to connect with the kidney pelvis. The kidney was drained as was the suppurative area around it. The convalescence of this patient was very interesting but that is another story. He is now well, having clear normal urine from both ureters.

DEMONSTRATION OF A NEW COMBINED CYSTOSCOPIC AND X-RAY TABLE¹

HUGH H. YOUNG

Baltimore, Maryland

I wish to bring to the attention of the members of the Association, a new urological examining table, which I have been developing in the workshops of the Brady Institute during the past three years and which is now perhaps sufficiently perfected to be worthy of demonstration before the Society.

For many years I have felt keenly the need of an X-ray table, which would be convenient for cystoscopy, so to avoid the difficult and tedious transportation of patient from cystoscopic to X-ray room. The table which I have brought before you is primarily an excellent urological table, both for operating and for cysto-urethroscopic work (figs. 1 to 6). It is well fitted for the best positions for cystoscopic work.²

Being provided with movable leg rests and capable of being changed by a simple rotating wheel to various positions, either horizontal or with head greatly depressed or elevated to an almost vertical position, it is suitable for cystoscopy with patient in various inclinations on the table. In the most dependent position (fig. 5) the bladder may be filled with air by negative pressure through an open cystoscope according to the method of Luys or of Kelly. A drain pan to collect drainage is provided. This remains in a horizontal position as the table is moved up or down in various positions. Shoulder rests which are movable and operated by a crank handle at the end of the table, make it possible to move the patient up or down upon the table even

¹ Read at the meeting of the American Urological Association, New York, April, 1920.

² The photographs are from a model made by Kny-Scheerer Company from original patterns made in Brady workshops.

when in a dependent posture. The X-ray part of the table consists of the usual upright cylinder, which slides upon horizontal tubular tracks attached to the cystoscopic table. Upon the upright cylinder, the tube holder is attached and is supplied with the usual stops or brakes, so that proper positions for satisfactory X-rays are accurately obtained. Numerous mechanical simplifications have been inserted and will be appreciated by radiologists. I will not, however, dwell upon these here.

The accompanying illustrations will show sufficiently well the mechanical structure of the table and various positions which can be procured.

In taking radiographs the patient is usually first placed in the horizontal position, the plates being inserted in the holder beneath the aluminum top of the table as shown in figure 3. This holder may readily be lowered for the removal and insertion of new plates and is easily moved so as to obtain the exact position desired. The pyelogram may be taken first in the horizontal position (fig. 3), then in the markedly elevated position (fig. 6) and finally in the markedly depressed position (fig. 5). In this way the entire excursion of movable kidneys is shown. Steroscopic pictures can be made in any position and are particularly valuable in differential diagnosis between ureteral calculi and phleboliths. For radiographs of the bony pelvis, including the bladder, lower ureters, seminal vesicles, vasa deferentia and prostate, the X-ray plate is placed lower down. Excellent shadowgraphs of the seminal vesicles and vasa deferentia, which I have been able to inject with thorium nitrate through a urethroscope are easily procured (fig. 7). This procedure brings up a new field for diagnostic study of diseases of seminal vesicles and vasa deferentia and in determining the question of sterility due to stricture of the seminal tract.³

The table shown in the accompanying illustrations therefore presents the following features: A cystoscopic table, in which the back rests upon a flat aluminum back plate, capable of being moved through a large arc from an extremely depressed to an

³ Johns Hopkins Hospital Bulletin, vol. xxi, 374, January, 1920.

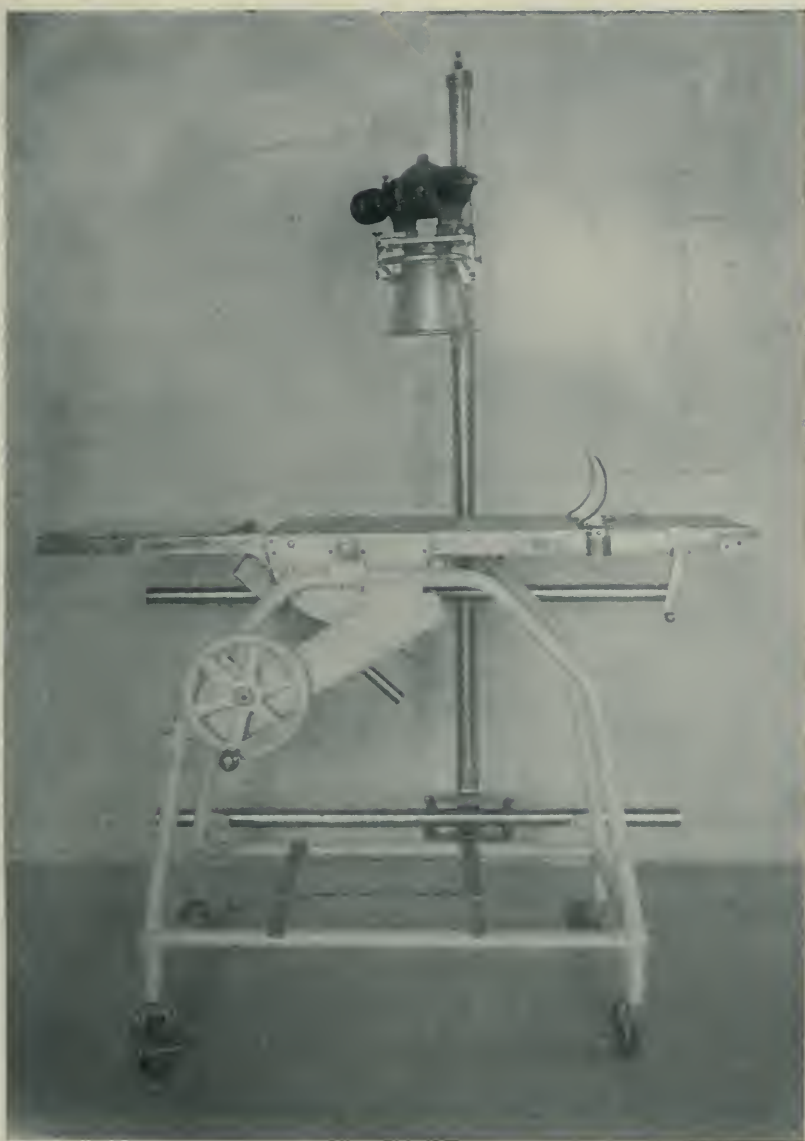


FIG. 1

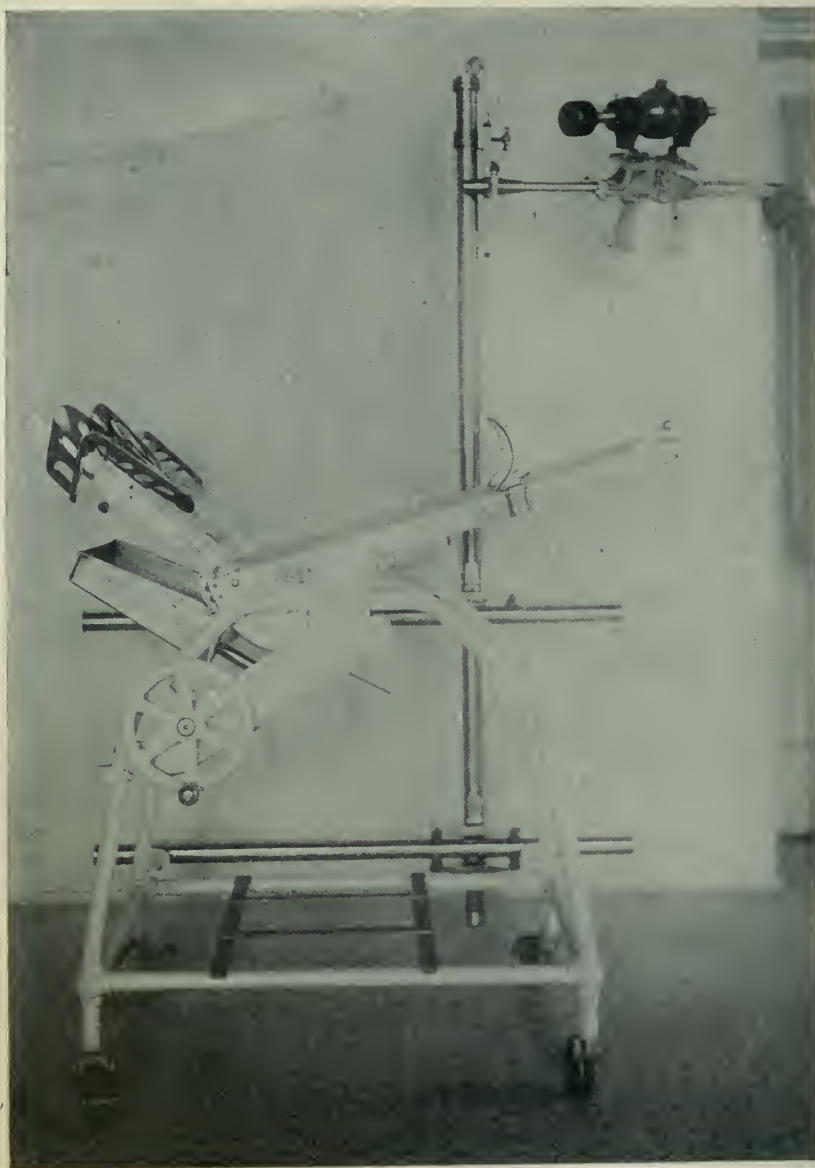


FIG. 2



FIG. 3



FIG. 4

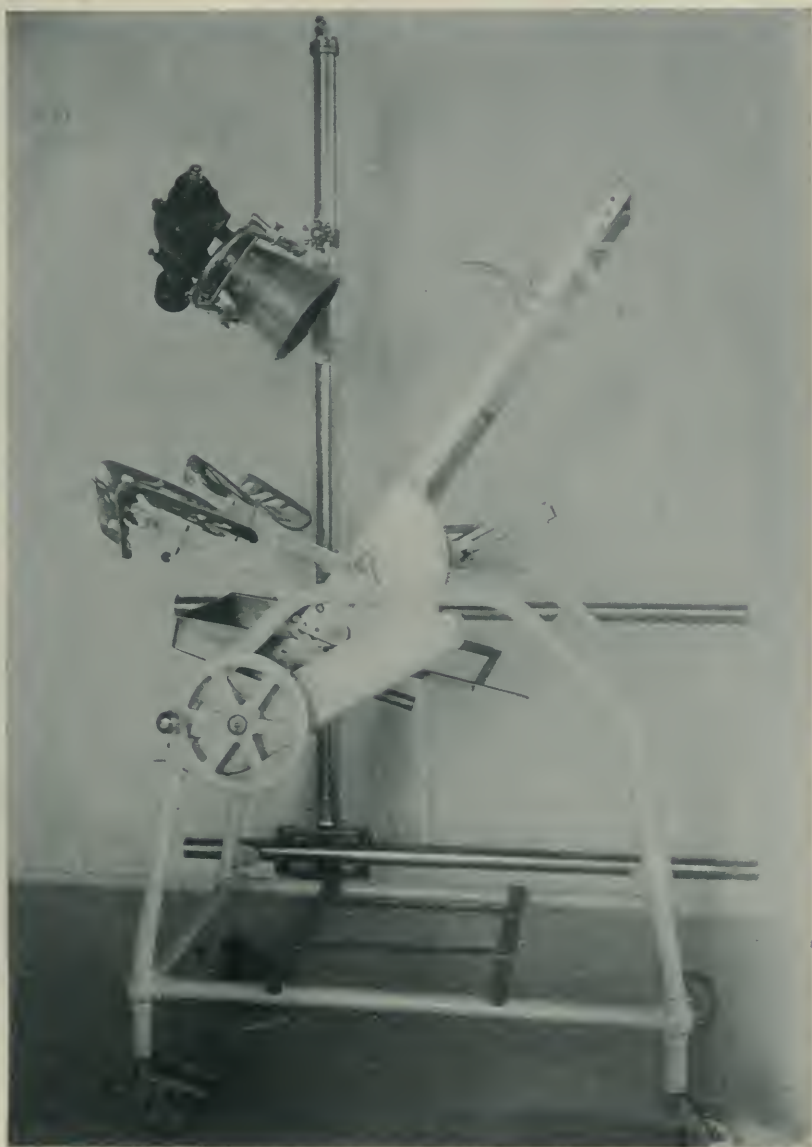


FIG. 5

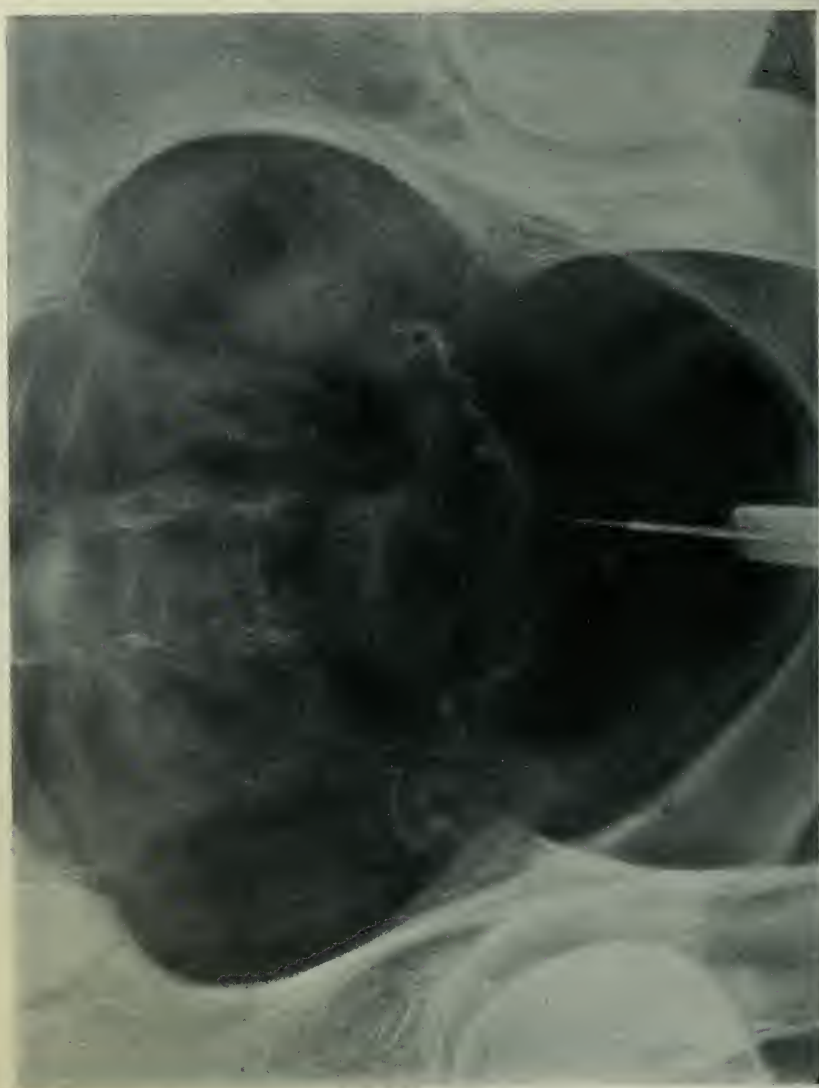


Fig. 6



FIG. 7



FIG. 8



FIG. 9



FIG. 10

almost vertical position. Leg rests which can be moved very easily and are so strongly constructed that the patient may sit upon them when in the upright position. Movable mechanically operating shoulder rests, by means of which the patient's position can be changed at will. A drainage pan, which remains in a horizontal position, while the table changes its position, but does not interfere with manipulation of X-ray plates beneath the table top. An X-ray attachment which gives great facility of movement and provides a simplified mechanism for stereographs.

The same table without the X-ray attachment has been arranged for urological operations of all characters and is especially valuable in obtaining a good position for operations through the perineum, upon the urethra and prostate (figs. 8-11). In addition, there is provided a pelvic elevator, which gives the proper inclination of the pelvis for a good exposure of the prostate through the perineum. In this position the knee crutches are removed and leg holders covered with large rubber tubes to prevent injury of the thighs while in this position (fig. 11). This table is particularly valuable in perineal prostatectomies upon very aged men, because they can be changed from the horizontal position, in which they are etherized, to the perineal position by very simple mechanical procedures. It is simply necessary to elevate the leg rests, while the etherizer turns the crank, which operates the shoulder rests. The perineal elevator is operated automatically by the movements of the shoulder rests and the perineal position is thus readily secured, with minimum disturbance to the patient. For operations upon the genitalia (epispadias, hypospadias etc.), upon the testicle and epididymis great facility is afforded in that the operator may stand or sit between the separated thighs of the patient (fig. 9). In combined suprapubic and perineal operations and in the radical operation for removal of the seminal tract in tuberculosis, the rapid facility with which the position of the patient can be changed from the perineal (fig. 11) to the horizontal (fig. 9) is of the greatest help. For kidney operation, a simple device for elevating the loin has been provided. It is operated by a double screw mechanism, lies on top of the table and is easily removable,

thus doing away with the usual bunglesome permanently attached apparatus. A recent addition consists of flat disc-like attachments on the shoulder rests, by means of which the chest can be held with one shoulder up in a vertical position during nephrectomy, thus doing away with the necessity of having an assistant to hold the body in the proper position, while the patient is on his side during the kidney operation. For suprapubic bladder operations, the exaggerated Trendelenberg position can be obtained, with the greatest ease. The legs being separated and the knees hooking over the crutches this position facilitates combined intra-rectal, vaginal, perineal and vesical manipulations. It is of assistance in suprapubic prostatectomy when the operator wishes to insert the finger into the rectum or when urethral or perineal instrumentation is desired. It is also valuable in cases of perineo-vesical fistula.

In this paper no attempt has been made to describe in detail the many new mechanical features embraced in this table and its attachments but perhaps it will suffice to indicate its usefulness for urologic examinations, cystoscopy with both water and air, urethroscopy, urological radiography ("urography"), and the varied operations of the genito-urinary tract.

A CASE OF PSEUDOHERMAPHRODISMUS MASCULLINUS, SHOWING HYPOSPADIAS, GREATLY ENLARGED UTRICLE, ABDOMINAL TESTIS AND ABSENCE OF SEMINAL VESICLES

HUGH H. YOUNG AND JAMES R. CASH

From the Brady Urological Institute, and the Department of Pathology, Johns Hopkins Hospital and University

This unusual case studied in the Brady Clinic and later in the pathological laboratory seems worthy of report:

Patient male, twenty-four years of age, single. Entered hospital July 15, 1918, and again on January 20, 1919 and December 16, 1919, for operations for hypospadias. His family and personal histories were negative except for present illness. He had had no urinary symptoms, normal sexual desire and erections, but had been unable to have satisfactory intercourse on account of contracture of penis. Five years ago, he had an operation to straighten contracture of penis. Operation presumably was a "Miculicz," transverse incision through skin and corpus spongiosum with longitudinal suture. Shortly after this a second operation was done by the same surgeon and an unsuccessful attempt was made to form a urethra. No history of venereal infections. Plastic operations of a preliminary character were performed on the first and second admissions to hospital.

Third admission. Nothing uneventful had occurred since patient's last admission in 1918. When he had an erection, the pendulous portion was still bent downward. Patient thinks erections have not been quite so firm as they used to be.

Examination. The patient presented a peculiar appearance. He was distinctly undersized and underdeveloped for a man of twenty-four years, and had much less hair on face and body than normal, but the shape of the body and appearance of the mammae were masculine in type. The penis was 3 inches long and had been unsuccessfully operated upon four times for hypospadias. The urinary meatus was at the peno-scrotal junction. The scrotum contained no testes or cords, was bifid in character and presented the appearance of labia majora,

but no suggestion of labia minora. Examination of the inguinal canals showed no testes and external rings were small. Distance from urethral meatus at the peno-scrotal junction, to the bladder was apparently $3\frac{1}{2}$ inches. On rectal examination the prostate could not be made out. Running from the region of the prostate, upward and toward the right, was an indefinite mass, which ended in a fine cord, which extended upward and along the posterior surface of the bladder. Urethroscopy showed a verumontanum but it was impossible to find the ejaculatory ducts or to introduce probes into ducts or utricle. X-ray plates showed delayed ossification at epiphyses—the picture of a boy of sixteen years. Head and cells negative. Bony skeleton of masculine type. It was thought wise to first perform a laparotomy to search for testicles and see if they could be transplanted in the scrotum and also to carry out operation to cure the hypospadias.

December 19, 1919. Operation. Young. Gas, oxygen and ether. (1) Laparotomy to search for testicles. (2) Perineal section for drainage. Rubber catheter sewed in. (3) Plastic operation to cure hypospadias by principle of Duplay.

(1) Median abdominal incision. Patient in the Trendelenberg position. Pelvis emptied of contents and search made for testicles. They were not present in the inguinal canals or pelvis. No search made in the region of the kidneys or above the bony pelvis. Careful examination of the posterior surface of the bladder was made and seminal vesicles were not visible but on each side a small cord, which ran upward and outward toward the lateral wall of the pelvis was found and thought to be the vas deferens. Abdomen was closed without drainage.

(2) A small incision was made in the perineum, opening urethra and a small catheter was introduced to drain the bladder. Catheter fastened into position by sutures.

(3) Plastic operation to close hypospadias by the method of Duplay. Incision made on each side of the mid-line, through the skin, from glans backward and around the urethral meatus in perineum. (Technique of this operation is shown in the accompanying illustrations figs. 1 to 4.) The skin was brought together around a small catheter with a continuous fine chromicized catgut suture, which did not include the epidermis. Glans penis was incised on each side and brought together continuous with the new urethra. Subcutaneous tissues were then brought together to reinforce and cover the new urethra, a continuous chromicized catgut being used. The skin was then drawn together by means of a horse hair mattress continuous suture, as shown in illustra-



FIG. 1. SHOWING THE LINE OF INCISION FOR PLASTIC OPERATION

Note the perineal opening of the urethra, the small empty scrotal sac and the skin flap of previous operation in the middle of the penis.

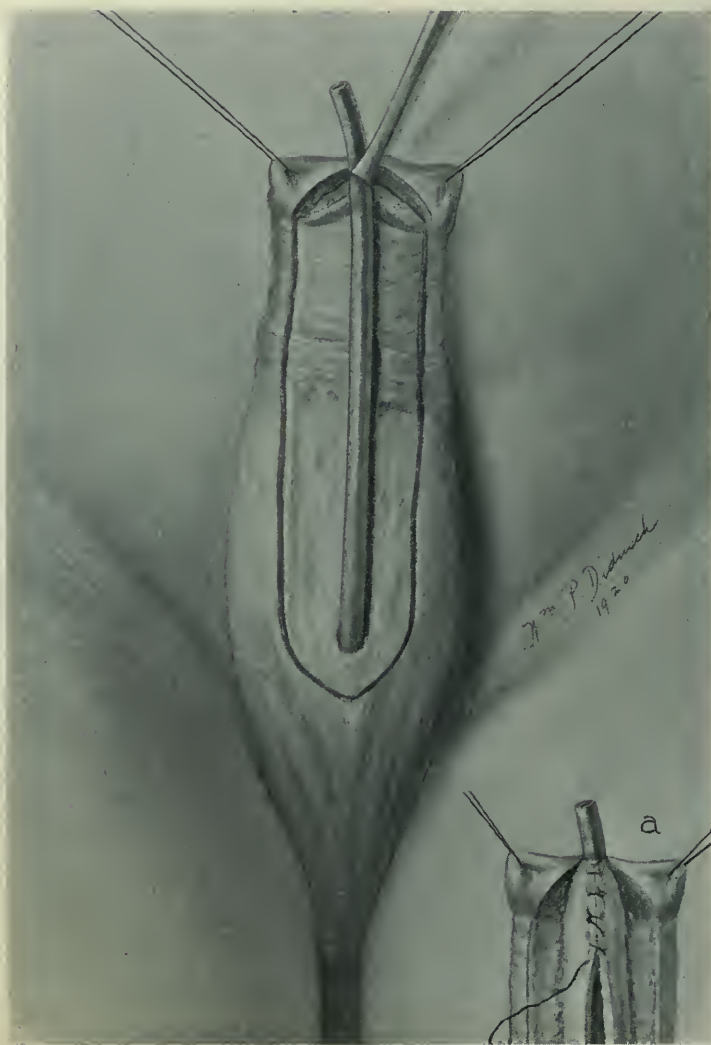


FIG. 2. INCISION CARRIED DEEPLY INTO GLANS

At *a*, the approximation of skin flaps to form urethra is shown.

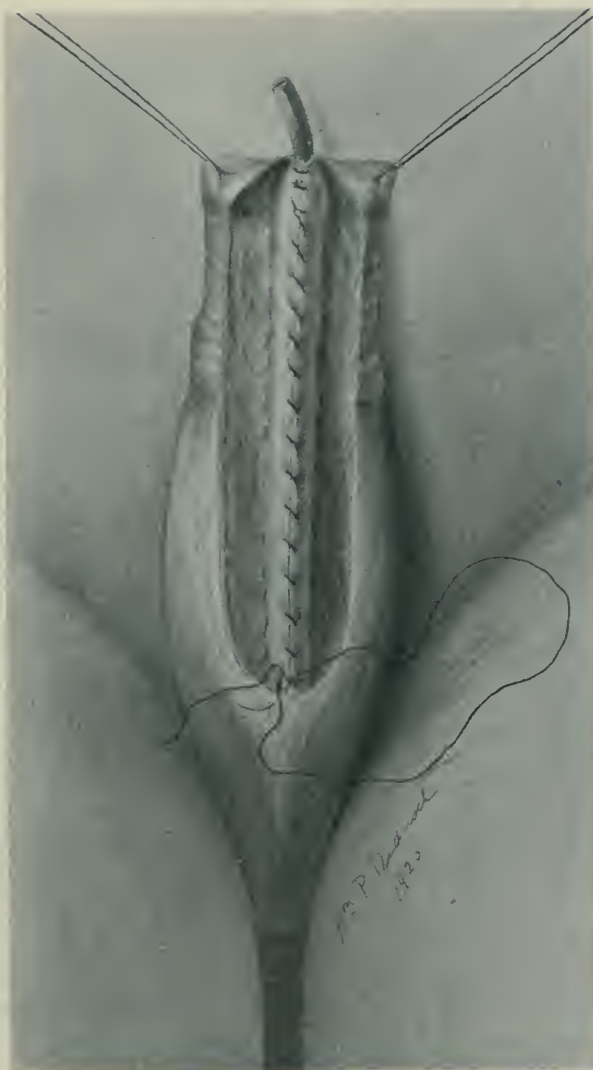


FIG 3. NEW URETHRA COMPLETED (FINE CHROMICIZED CATGUT SUTURE)

This suture is used to make the final closure

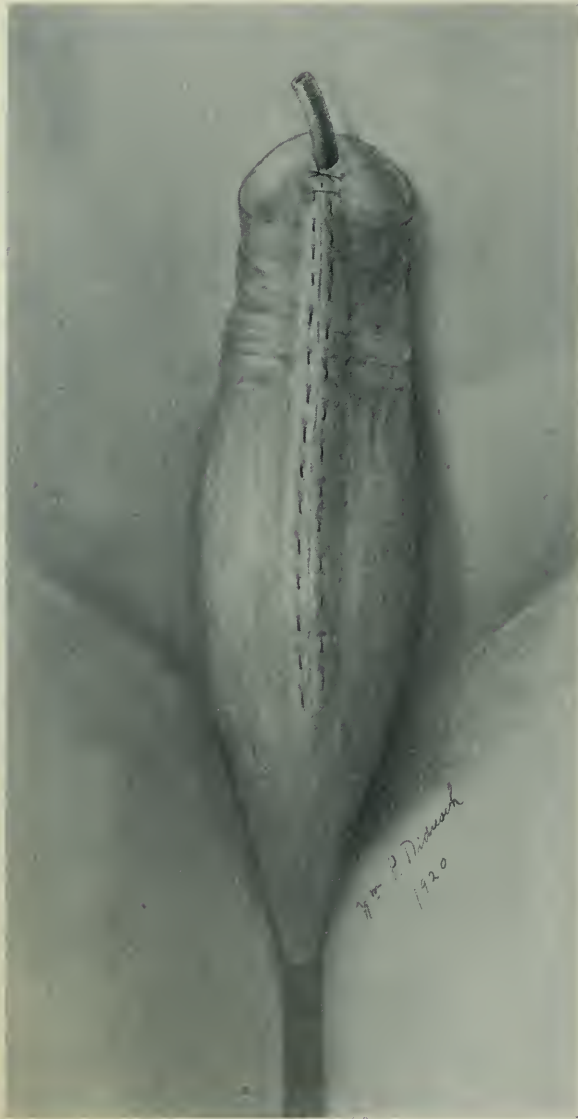


FIG. 4. COMPLETED OPERATION; CATHETER IS THEN REMOVED.

tions, thus forming a new urethra about $3\frac{1}{2}$ inches in length and very satisfactory in appearance. In order to relieve tension, a longitudinal incision was made along the dorsum of the penis and the wound was drawn together transversely with three stitches of catgut. The catheter which was used in making the new urethra was withdrawn at the end of the operation to avoid pressure necrosis.

Convalescence. January 2, 1920. It is now two weeks since the operation. Patient is still wearing a perineal drainage catheter, which is draining well. No urine has come through the anterior urethra. Operative wound has done well. There has been no general breakdown or suppuration. There are three small, pin-point openings, through which a slight amount of fluid escapes, when solution is injected into the new meatus. The new glandular urethra is entirely satisfactory. General condition excellent. It seems wise to continue the perineal drainage for a few days longer.

January 15, 1920. Patient voids about two-thirds of urine through the new formed urethra and one-third through the perineal fistula, which is still open. Several small pin-point openings in the new urethra are visible. Filiform and dilating followers up to 20F. are passed without difficulty into the bladder.

January 16. Patient complains of sore throat and coughs occasionally. Examination of the chest negative.

January 17. Temperature 101° . January 18, 102° . Throat cultures were made on January 20 and showed both hemolytic and non-hemolytic staphylococcus and a few days later influenza bacilli were also obtained. On January 24, 1920 temperature rose to 104° . Examination showed a bilateral broncho-pneumonia. On January 25, fluid was discovered on the left side and 1800 cc. of purulent fluid was removed by thoracentesis. January 27, 1920 1200 cc. of fluid was obtained, and thoracotomy was then done by Dr. Heuer for drainage. After this patient continued to grow worse and pulse became very rapid and temperature remained low. On January 30 the pulse became imperceptible and patient died.

Diagnosis. Influenza with bilateral broncho-pneumonia. Empyema, left side.

Autopsy

Body. The body is that of a well nourished young white man, weighing 51 kgm. and measuring 160 cm. in length. Rigor mortis is extreme.

The eyes, ears, nose and mouth show no features worthy of note.

Thorax. The thorax is well formed and symmetrical. In the left posterior axillary line there is a small opening into the pleural cavity; about 3 cm. of the 7th rib has been removed and from this opening a purulent exudate flows freely when pressure is made upon the left thoracic wall.

Abdomen. The abdomen is flat and the abdominal muscles in a state of rigor mortis. Just above the symphysis, in the midline, is a healed, linear scar 10 cm. in length.

External genitalia. The external genitalia present a very unusual appearance. The pubic hair is quite scanty and of a light color. Its arrangement, while not distinctly of the transverse or feminine type is, on the other hand not definitely of the triangular or masculine appearance. There is no well formed scrotum. A loose fold of wrinkled skin occupies this position. No testes can be felt within this fold, neither can they be felt higher up along the course of the inguinal canal. The penis is of usual size and shows a great many old scars both over its dorsal and ventral aspects. These scars are more numerous over its ventral surface and over this scarred surface a number of openings of old fistulae may be seen. These fistulae, five in number, connect with the lumen of the urethra, as pressure over the region of the bladder causes urine to jet forth from all of them.

Extremities, skin, external lymphatic glands. The extremities are well formed and show no abnormalities.

The hair over the trunk and extremities is very slight in amount. The beard and axillary hair are quite scanty.

A few cervical, axillary, and inguinal glands can be palpated but are not markedly enlarged. The epitrochlear glands cannot be felt.

Abdominal cavity. On opening the abdominal cavity the serous surfaces of the viscera are seen to be smooth and glistening and all of the abdominal organs are found to be approximately of normal size and to occupy their usual positions. On exploring the walls of the abdominal cavity and pelvis a small round mass suspended by a pedicle is found just below the lower pole of the right kidney (fig. 11). This mass measures about 2 cm. in diameter and is covered with peritoneum which extends down over its pedicle and is continuous with the general peritoneum; it is of slightly oval shape, almost round, and has a firm, rubbery consistency. Leading downward from the pedicle of this structure the peritoneum is thrown up into a small, flat fold about 1.5 cm. broad which becomes continuous with the peritoneal covering of the posterior

wall of the bladder. Between the layers of this fold of peritoneum, leading from the pedicle of the mass are several large blood vessels which disappear behind the bladder. On the left side of the abdominal cavity there is a similar fold of peritoneum in approximately the same position, however, no corresponding pedunculated mass can be found at its upper end which spreads out to form a flat fan-shaped fold with a denticulated edge. (fig. 11). This fan-shaped fold contains many blood-vessels between its layers and a small oval mass about 4 mm. in diameter which is situated near its free edge. The remainder of the fold leading to the back of the bladder carries large blood-vessels as does the corresponding fold on the right side and situated in it near its free edge at a point somewhat nearer its lower end is an oval mass about the size of a small pea. It is of a yellowish white color and of firm, rubbery consistency. By palpation no prostate or seminal vesicles can be felt in their usual positions.

Thoracic cavity. On removing the sternum the thoracic viscera are seen to occupy their usual positions. No thymus can be found. The left pleural cavity, which has been drained surgically contains about 10 cc. of fibrino-purulent exudate which covers practically the entire surface of the left lung. The left apex is fixed by several old adhesions. The right pleural cavity is free from fluid and exudate and its surface is smooth and shining.

Heart. Weight 260 grams. The heart shows no abnormalities.

Lungs. Left, weight 1040 grams. The left lung is quite large. Its lower lobe and the lower part of the upper lobe is of a dull, mottled, reddish-gray color and is covered by a fibrino-purulent exudate which also has bound the two lobes together. The upper part of the upper lobe is dark red and the pleura has a dull, smoked appearance. There are several old adhesions at the apex. The lower lobe of the lung is quite firm and contains very little air.

Most of the upper lobe, however, contains air but many firm areas may be felt within it. On section the entire cut surface is quite hemorrhagic. The upper lobe drips with blood and contains numerous circumscribed, dark red, elevated areas which do not contain air. The remainder of the upper lobe is quite moist but for the most part air containing. The lower lobe contains very little air and its cut surface shows many large, elevated, red confluent areas many of which show gray patches in their centers from which pus may be expressed. The large bronchi contain purulent exudate which may easily be washed off leaving a very highly injected wall behind. Pus may be expressed

from most of the smaller bronchi. The large pulmonary vessels are free from obstruction and their walls show no abnormalities but many of the smaller vessels contain thrombi. No infarcts of the lung can be seen.

Right lung, weight 780 grams. The right lung is quite voluminous. Its pleural surface is smooth and glistening and of light gray color slightly pigmented with coal dust. The two upper lobes are quite soft and air containing. The lower lobe is much firmer and appears to be mostly consolidated. On section the two upper lobes have a homogenous pink color and seem to contain air throughout. The surface of the lower lobe is of much darker red color and shows many large, elevated confluent consolidated areas. A few thrombi may be seen in the smaller pulmonary veins but no infarcts are evident. The bronchi of the lower lobe are highly injected and contain a purulent exudate.

The lymph glands at the hilum of the lungs are slightly enlarged but soft. They show moderate pigmentation with coal dust.

Liver. Weight 1920 grams. Both liver and gall-bladder are normal.

Pancreas. Weight 40 grams. The pancreas is of normal appearance.

Spleen. Weight 180 grams. The spleen is slightly enlarged but shows no other noteworthy features.

Stomach, duodenum and intestines. Normal. •

Abdominal lymph glands. All of these glands are of normal size, color and consistency.

Adrenals. Weight (together 18 grams) These organs appear normal.

Genito-urinary system (fig. 12). Kidneys: Left, weight 140 grams; right, weight 160 grams. Neither of the kidneys shows any macroscopic abnormality. The left ureter is of normal size; its lumen is free from obstruction and it pursues its usual course to the bladder. The right ureter is of normal size and free from obstruction but just before reaching the bladder it is displaced laterally by an anomalous structure (fig. 12) which lies on the right posterior aspect of the bladder and around which the ureter passes to empty into the bladder in the usual way.

Bladder. The bladder contains about 75 cc. of clear urine. It is of normal size and its wall of normal thickness. The epithelium lining the bladder is delicate and completely intact. The ureteral and urethral orifices are situated in their usual positions and unobstructed.

Prostate. No well formed prostate can be discovered on external examination of the dissected specimen. However, upon making a transverse cut across the urethra at the level of the usual position of the prostate, a considerable amount of glandular tissue resembling

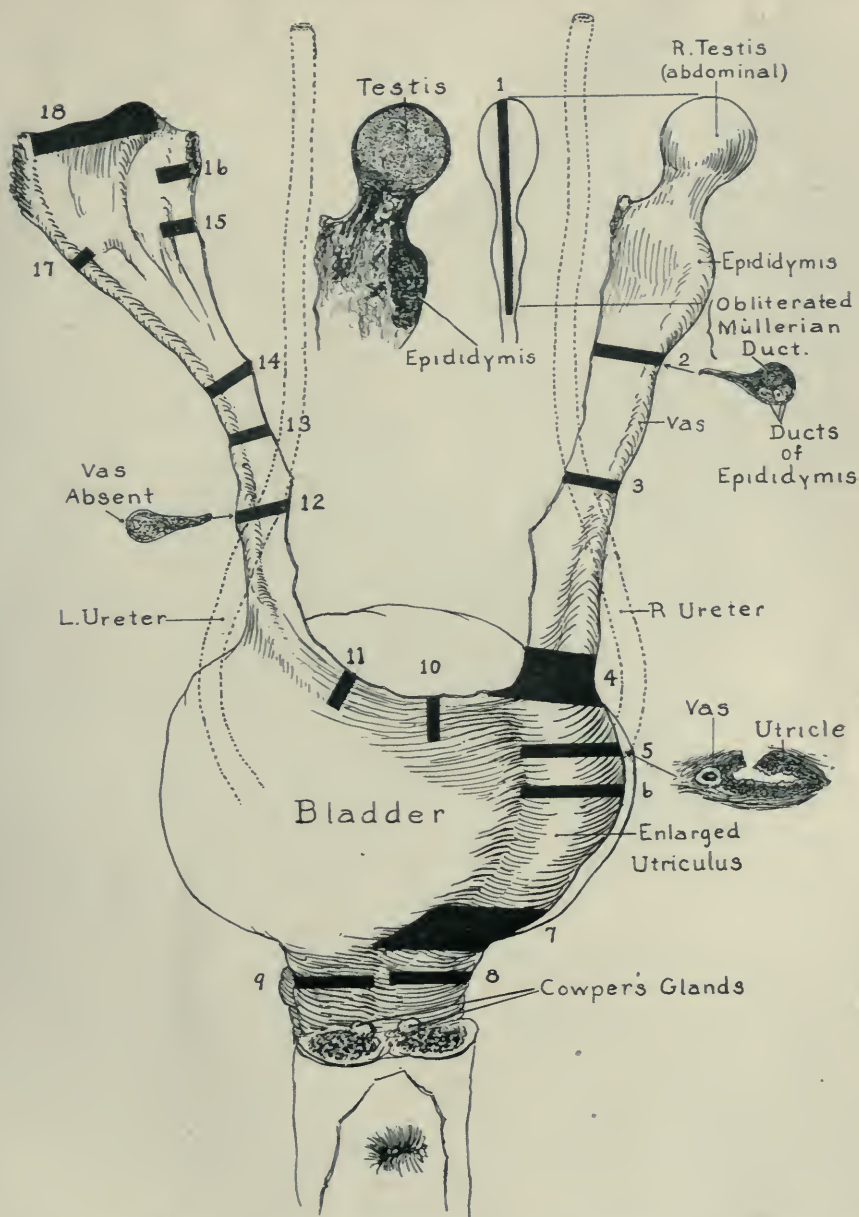


FIG. 5. DIAGRAM OF DISSECTED SPECIMEN VIEWED POSTERIORLY ILLUSTRATING THE LOCATIONS FROM WHICH THE MICROSCOPICAL SECTIONS DESCRIBED IN THE TEXT WERE TAKEN

prostate may be seen surrounding the urethra. Most of the prostate is situated dorsal to the urethra but a small portion lies lateral and ventral to it.

Seminal vesicles. No seminal vesicles are to be seen. However, lying on the posterior wall of the bladder approximately in the position of the right seminal vesicle, is an anomalous curved structure 7 cm. in length and 2 cm. in width at its broadest point (fig. 12). The structure becomes much smaller at its ends. The lower one of which appears to unite with the ventral aspect of the membranous urethra while the upper one becomes continuous with the ligament of peritoneum leading from the small pedunculated mass in the right side of the abdominal cavity to the back of the bladder.

Urethra. On opening the urethra along its dorsal surface an imperfectly formed lumen is found throughout its entire extent. This lumen is practically obliterated by scarring about 3 cm. from the meatus. There are numerous small fistulae and false passages which open externally along the ventral side of the penis.

Anomalous structures associated with genito-urinary tract (figs. 11 and 12). The round mass covered with peritoneum and situated at the upper end of the narrow fold of peritoneum extending from near the lower pole of the right kidney to the bladder, measures 2 cm. in diameter. It is quite firm and elastic and receives several good-sized blood-vessels by way of the small, flat stalk of peritoneum by which it hangs. The structure has the general appearance of a testicle and situated, adjoining it in the stalk from which it hangs is a small elongated mass of glandular tissue which appears to be epididymis. Extending down the main fold of peritoneum continuous with the epididymis is a small, firm cord-like structure, about 4 mm. in diameter which becomes continuous with the anomalous, curved structure situated on the posterior aspect of the bladder.

On opening this anomalous structure fig. 12 (c) it is seen to be a single tube with quite a thick, muscular wall and lined throughout with epithelium. Its lower end opens by a small orifice into the floor of the urethra at the verumontanum in the position of the utriculus. In fact, this entire anomalous structure may very well be a greatly enlarged utriculus. Its upper end, at first sight, appears to end blindly but careful examination reveals a very small opening, much too small to admit the point of the finest probe. The lining of this structure is smooth and regular except for one area of the side next to bladder where a small longitudinal ridge about 2 cm. in length in its wall is seen

(fig. 12 (c)). In the distal end of this ridge a minute opening is seen. A transverse cut was made across this entire structure down to the bladder wall through the middle of this ridge and the cross section of a duct about 1 mm. in diameter and possessing a definite wall of its own is seen lying within the thick wall of the anomalous tube just opposite the small ridge seen on its interior (fig. 5 (6) fig. 9). A similar transverse section made below the distal end of the ridge failed to show any such duct in cross section (fig. 5 (7)). A very fine probe passed into the duct goes in the direction of the small opening seen in the distal end of the small ridge but cannot easily be forced through it. Several trans-

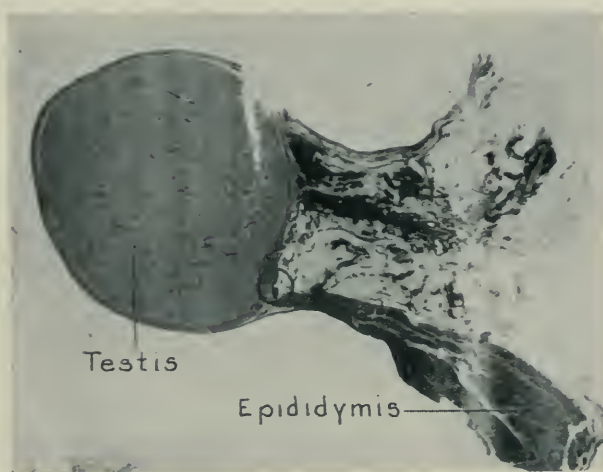


FIG_6. SAGGITAL SECTION THROUGH TESTIS AND EPIDIDYMIS (LOW POWER),
FIGURE 5 (1)

verse cuts made across the large tube at higher levels show the same duct lying between it and the bladder. At the upper end of the tube, however, this duct breaks up into three smaller ducts similar to it in appearance all of which pass together up between the folds of the ligament of peritoneum to the epididymis of the testicle with which they appear to unite (fig. 5 (4) fig. 7).

Accompanying these ducts in the ligament of peritoneum is another small duct continuous with the lumen of the large anomalous tube just described. This duct persists only for 6 or 8 cm. from the upper end of the tube and finally become obliterated into a cord of fibrous tissue which accompanies the aggregation of small ducts leading to the epididy-

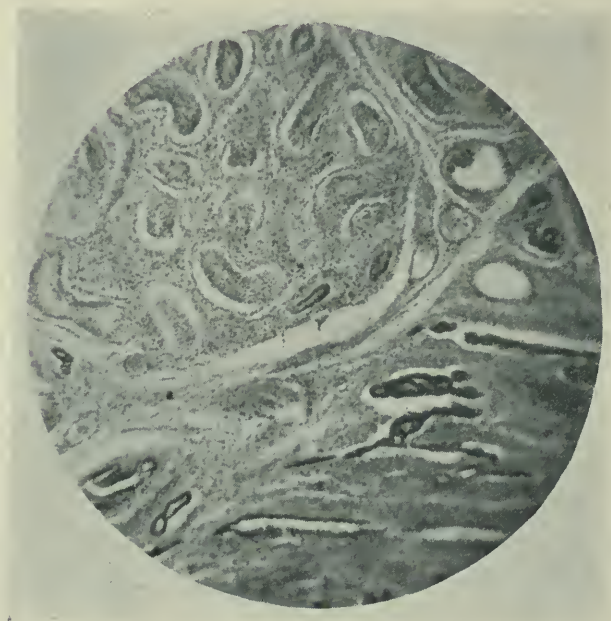


FIG. 6A. HIGH POWER FIELD AT JUNCTION OF EPIDIDYMIS AND TESTIS

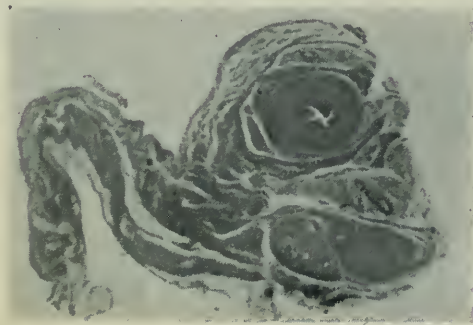


FIG. 7. TRANSVERSE SECTION AT UPPER END OF ENLARGED UTRICULUS,
FIGURE 5 (4)

The larger duct standing alone is the utriculus and the aggregation of smaller ducts are those of the epididymis which persist down to this level (low power).

mis. Several large blood-vessels also are included in this fold of peritoneum along with the ducts described.

The fold of peritoneum lying on the left side of the body in similar position to the one just described is found to contain only a few blood-vessels and two small, yellowish, firm nodules, one at the upper, free end and another at the edge of the fold at about two-thirds of the distance from its upper end to the bladder. These are each about 3 mm. in diameter and lie apparently unconnected with any other significant structure. No testicle, epididymis, vas deferens or other unusual structures are to be seen associated with this fold of peritoneum or are any of these structures found anywhere on the left side of the body.

Microscopic notes

Lungs. A section from the left lung shows the pleura to be slightly thickened and covered by a thick exudate composed of fibrin, polymorphonuclear leucocytes and coagulated necrotic material. Great areas of alveoli and many bronchi are filled with a similar exudate which greatly distends many lymphatics in these areas. In other areas the alveoli are full of coagulated fluid. Numerous alveoli and capillaries are plugged with fibrin but the larger blood vessels are free from thrombi. A few air-containing alveoli are seen. Great clumps of bacteria (streptococci) are seen throughout the section.

In the section taken from the lower lobe of the right lung many alveoli and bronchi are seen to contain exudate similar to that described in the left lung. The pleura, however, is unaltered and there are many more air-containing alveoli than in the left lung. A section from the right upper lobe is essentially normal.

Liver and kidneys. Cloudy swelling.

Heart, spleen, pancreas and adrenals. Normal.

Genito-urinary tract. (See fig. 5 for positions from which sections were taken and figs. 6 to 10 for photomicrographs.)

1. Testes. Figure 5 (1); figures 6 and 6a. The seminiferous tubules have their usual general shape and arrangement but they are lined by several layers of undifferentiated cubical epithelium. Some apparently have no lumen at all and the lumen of the majority of tubules is quite small. No evidence of actual spermatogenesis is seen. However, in the lumen of a few tubules there are small, dark staining bodies which suggest poorly formed spermatozoa. The basement membrane of all the tubules is quite thick. The interstitial tissue is abun-

dant and contains a great many large pale staining, polygonal cells (Whitehead 1). The blood-vessels of the testis show no abnormality.

Associated with the testis there is shown in this section a well formed epididymis. Its epithelial lining shows nothing unusual and its convolutions are normally arranged. Only a few desquamated epithelial cells and a little coagulated fluid is seen within the lumen of the epididymis.

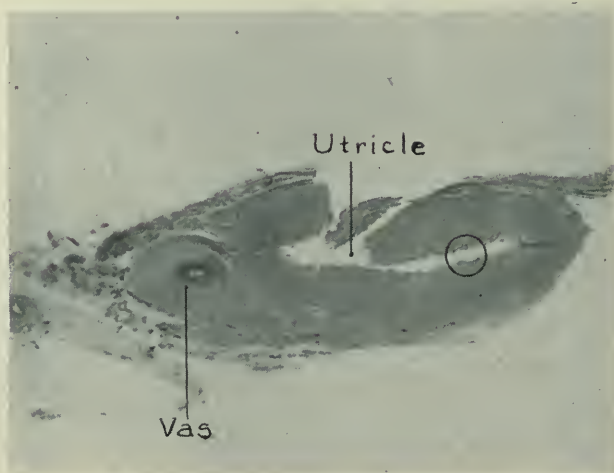


FIG. 8. TRANSVERSE SECTION TAKEN AT UPPER PART OF ENLARGED UTRICULUS, FIGURE 5 (5)

The small duct lying adjacent to the utriculus is the vas deferens. At the upper end of the utriculus it becomes continuous with the ducts of the epididymis. The vas opens into the utriculus near its lower end (low power).

2. Transverse section just below the epididymis. Figure 5 (2). A definite cord of fibrous tissue containing a few small blood vessels is seen in cross section. There are twelve much smaller ducts which anastomose freely just lateral to the fibrous cord. These ducts are lined with a single layer of cubical epithelium and have thin muscular walls. The fibrous cord is taken for the obliterated Müllerian duct while the smaller ducts may be traced in serial section to their junction with the epididymis.

3. Transverse section across right fold of peritoneum at its middle point. Figure 5 (3). This section shows a very small duct in cross section and another much larger structure composed of a thick wall of

smooth muscle and connective tissue in the center of which is an irregularly shaped lumen lined with columnar epithelium over part of one side and showing a marked proliferation of the cells of its wall which bulge out into the lumen from the other side. It appears as if the lumen has become partly obliterated. This structure we take for the remains of the Müllerian duct. It is this structure which forms the firm cord which may be felt in the fold of peritoneum leading from the testis.

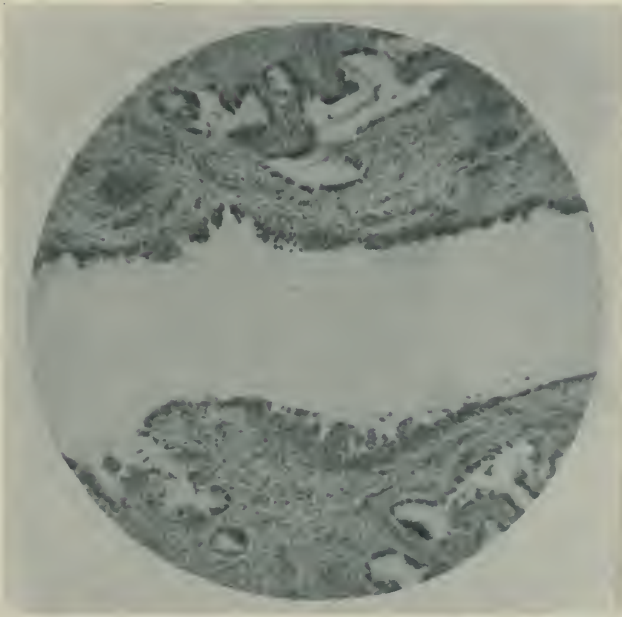


FIG. 8A. HIGH POWER FIELD OF LUMEN OF UTRICULUS SHOWING ITS MUCOSA COMPOSED OF STRATIFIED EPITHELIUM AND NUMEROUS GLANDS LINED WITH COLUMNAR EPITHELIUM WITHIN ITS WALL

The loose character of the stroma is also shown

The other structure mentioned above in this section is a well formed small duct with a much convoluted epithelial lined lumen. It is evidently one of the numerous anastomosing tubules seen in the above section 2 as it resembles them quite closely in every respect.

The remainder of the section is composed of areolar tissue, and blood vessels which lie around these structures just mentioned between the two layers of peritoneum. Their arrangement does not appear to be of any significance.

4. Serial sections taken at upper end of anomalous tubular structure on back of bladder. Figure 5 (4); figure 7. This structure has a thick muscular wall not unlike uterus in its appearance. However, it is lined with stratified epithelium which dips down into its muscular wall to form many glands most of which are lined with a single layer of cubical epithelium. As this structure is followed upward its lumen becomes quite small and its lining becomes a single layer of columnar

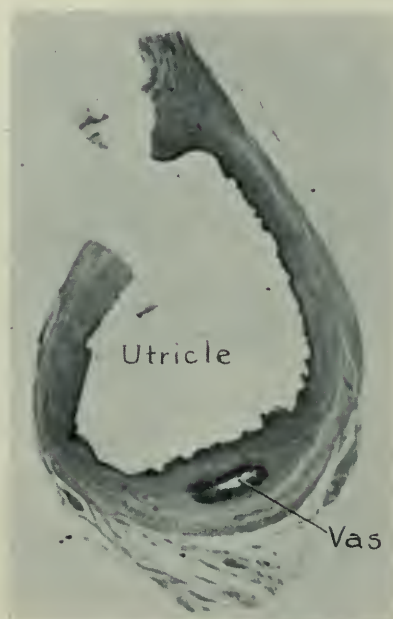


FIG. 9. TRANSVERSE SECTION THROUGH UTRICULUS AT SOMEWHAT LOWER LEVEL, FIGURE 5 (6)

The vas deferens is seen within the wall of the utriculus (low power)

epithelium resembling closely the remnants of columnar epithelium seen with the ill-defined lumen of the fibrous cord, seen in section 3 and which is seen microscopically, to be the continuation of the structure we are now describing.

Situated just to one side of this structure there is seen in these sections a number of anastomosing ducts varying from three to eight. They have thick muscular walls and convoluted lumens whose lining epithelium is quite similar to that of the numerous anastomosing ducts

seen in section 2 described above. In fact, these ducts resemble those in the above section in all respects except that they are fewer in number and much larger.

5. Transverse section taken just below 4. Figure 5 (5); figures 8 and 8a. At this level the resemblance of this anomalous structure to uterus is much more striking than in the previously described series of sections. The wall is composed of a thick layer of smooth muscle and connective

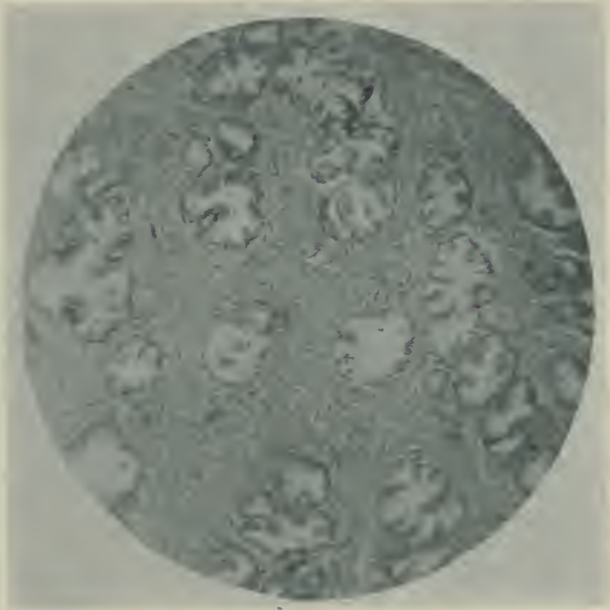


FIG. 10. RUDIMENTARY PROSTATE, FIGURE 5 (8)

tissue which, at a point about midway between the exterior and the lumen of this structure, gradually merges into a stroma of small homogeneously arranged, loosely packed, cells quite similar to those seen in the uterus. They are in general of short spindle-shaped type and have quite scanty cytoplasm with prominent round or oval, irregularly staining nuclei. The lumen is lined with many layers of stratified epithelium which dips down into the stroma and assumes in many places, a gland-like arrangement. The epithelium lining these glands, however, is of the columnar form.

Situated just laterally to this structure there may also be seen in the section an entirely separate much smaller duct lined with epithelium and having a very thick wall composed of fibrous tissue and smooth muscle. The walls of these two structures merge into each other on their contiguous surfaces. The lumen is much denticulated by long branching strands of the surrounding stroma which project into it. All of these are covered with several layers of cubical epithelium. This structure we take for the vas deferens.

6. Transverse section taken 1 cm. below 5. Figure 5 (6); and figure 9 (*low power*). This section shows the same structures as does section 5. The vas deferens however, has become incorporated in the wall of the enlarged utricule.

7. The lumen of the utriculus has become much smaller but its lining epithelium and wall have the same characteristics as seen in the sections taken at higher levels. The vas deferens opens into the utriculus between the levels of 6 and 7 and therefore is not shown in the series of sections taken at 7.

8 and 9. Sections taken from the neck of the bladder at these points are composed mainly of rudimentary prostatic tissue. Attention is again called to the absence of seminal vesicles and ejaculatory ducts. Figure 5 (8-9); figure 10.

10, 11, 13, 14, 15, 16, 17, 18. Numerous sections taken from these sites fail to show any noteworthy structures. No ducts, similar to those described on the right side are to be found and sections 14 and 11 show there are no connections between the right and left folds of peritoneum.

12. Section through small nodule in left anomalous fold of peritoneum. figure 5 (12).

This is a very vascular group of nondescript cells. They are quite small and irregular with non-distinctive nuclei. No features of the section suggest either testis or ovary.

Anatomical diagnosis. Malformation of genital organs; undescended and imperfectly developed testis (right), greatly enlarged utriculus, rudimentary prostate, absence of left testis and seminal vesicles, hypospadias; surgical treatment of hypospadias with remaining urethral fistulae; confluent lobular pneumonia (*streptococcus haemolyticus*); surgical drainage of empyema (left.)

DISCUSSION

The relation of this case to hermaphrodisism requires some consideration. While there are no definitely female parts the hypospadias, enlarged uterus masculinus, partially obliterated Müllerian duct show the tendency toward feminine development. The following classification of the different forms of hermaphrodisism is by Marchand (2):

A. *Hermaphrodisimus Verus*, i.e., the existence of both male and female sexual glands in same body. Of this group there are three subdivisions:

(1) *H. lateralis*, denotes the presence of any ovary on one side and a testis on the other.

(2) *H. semi-lateralis*, describes that condition where both an ovary and testis exist on one side and either or niether on the other.

(3) *H. bilateralis*, denotes the presence of both ovary and testis on each side of the body.

B. *Pseudohermaphrodisimus*, i.e., the rudimentary development of the sexual glands while, at the same time the external genitalia are more or less altered and the secondary sexual characteristics, i.e., voice, growth of hair, dimensions of skeleton are reversed.

Of this group to which belong most anomalies of the genital tract there are two types:

(1) *Pseudohermaphrodisimus Masculinus*. Here the sexual glands, though rudimentary are masculine while the rest of the internal genitalia and the external genitalia are more or less feminine.

(2) *Pseudohermaphrodisimus Femininus*. Here the sexual glands though rudimentary are feminine while the other genitalia and habitus are more or less masculine.

Pseudohermaphrodisism is much more common than true hermaphrodisism and pseudohermaphrodisism masculinus by far the most common type. Marchand (2), states that its occurrence with hypospadias, an enlarged utriculus (uterus masculinus) rudimentary prostate, and undescended testicle is not uncommon and that in these cases the Wolffian duct (vas deferens) empties either into the enlarged utriculus or floor of the urethra.



FIG. 11. DRAWING OF ABDOMINAL CAVITY WITH INTESTINES AND PERITONEUM REMOVED
SHOWING THE ABDOMINAL TESTICLE AND EPIDIDYMIS WITH THEIR ASSOCIATED
FOLD OF PERITONEUM

The fold of peritoneum found in similar position on the opposite side is also shown.
The hyospiadias is represented as it existed before operative procedures were undertaken.



FIG. 12. DRAWING OF POSTERIOR VIEW OF INTACT DISSECTED SPECIMEN.

a, Testis and epididymis, *b*, denticulated anomalous fold of peritoneum testis, epididymis and vas absent; *c*, interior view of enlarged utericle opened longitudinally, *d*, opening of utericle into floor of membranous urethra; *e*, Cowper's glands; *f*, ventral aspect of penis after operation for hypospadias; *g*, enlarged utericle.

This last mentioned group of associated conditions bears a striking analogy to the present case under consideration and were external genitalia and habitus more of female type, it would certainly afford a typical example pseudohermaphroditismus masculinus. However, as it stands, this case more closely approximates this type of malformation of the genital system than any other.

Many similar cases are to be found in the literature. Arnold (3), reports a case of a seven months foetus whose premature birth was probably caused and greatly interfered with by a large abdominal tumor. The child was removed in pieces. The tumor proved to be the greatly dilatated bladder which was associated with a large uterus masculinus and stricture of urethra. Arnold, also reports 26 cases of uterus masculinus which are authentically proven and represent all such cases reported to that time. From the study of his summary of these cases it appears that the uterus masculinus may be a small pocket, or a definitely anomalous organ either solid or with a canal of varying diameter. It may be a double stricture but generally exists as the partial or complete fusion of the lower ends of the Müllerian ducts. In accordance with the statement of Marchand, Arnold finds hypospadias, anomalous scrotum and penis; undescended testes, rudimentary or lacking seminal vesicles and prostate as associated conditions with enlarged uterus masculinus. Stroebe (4) reports a typical case of pseudohermaphroditismus masculinus internus with good histological descriptions. Benda (5) contributes an excellent discussion of hermaphroditism and malformations with changes in sexual characteristics.

Two cases recently studied at the Johns Hopkins Hospital are those of Cullen and Quinby. Cullen (6) reports the case of an adult individual with rudimentary vagina and penis having a urethra of feminine type. All of the secondary sexual characteristics, e.g., hair, voice, and skeleton, were masculine. Laparotomy failed to reveal any uterus, tubes, or ovaries but a well-formed testis and epididymis were found in a hernial sac. Microscopical examination showed the testis to be

non-functioning. Quinby (7) describes a person 10 years of age with rudimentary penis, labia majora, and hypospadias. The pubic hair was of feminine type but the other secondary sexual characters masculine. No prostate could be palpated or any testes found by external examination. Laparotomy revealed well formed uterus, tubes and ovaries but no trace of testes could be found.

Although these cases were not studied by autopsies the surgical findings establish the diagnosis. It is at once seen that they represent the two most common types of pseudohermaphrodisim, the former being one of pseudohermaphrodisim masculinus while the latter illustrates pseudohermaphrodisim femininus.

SUMMARY

It appears in the development of the urogenital system of this individual, that a tendency toward hermaphrodisim has been shown. However, on the whole, the organs are those of a masculine person though much altered in morphology and function. Briefly, the situation is this:

On the right side just below the kidney there is a non-functioning, undescended testicle continuous with which is a well defined epididymis (figs. 11 and 12). The epididymis persists as a group of anastomosing tubules, all of which pass together down a fold of peritoneum to the right posterior wall of the bladder. At this point these tubules converge to form one larger duct which is considered to be the vas deferens. This structure runs along for 5 cm. between the posterior wall of the bladder and an anomalous curved tube which lies adjacent to it and into the lower end of which the vas deferens opens by a narrow orifice (fig. 12) (c). This anomalous structure is taken to be a malformation of the utriculus because of the following points: (1) Its wall and epithelial lining resemble closely that of the uterus (figs. 8 and 8a); (2) Its lower end opens into the floor of the urethra in the position of the uterus masculinus (fig. 12) (d); (3) Its upper end is in continuity with a small partially obliterated duct which is taken to be the remains of the embryonic predecessor of the uterus, the Müllerian duct.

On the left side of the body there is a fold of peritoneum similar to the one on the right but it contains no structures which may be identified as organs or remnants of embryonic structure. There are no connecting structures between the right and left folds of peritoneum.

The prostate is quite small but well defined both grossly and microscopically. No trace of seminal vesicles are found.

The following feminine characters are present: (1) A persistent, partially obliterated Müllerian duct exists on the right side forming, at its lower end, a greatly enlarged one-horned utricle. (2) There is a urethra of more or less feminine type.

If one chooses to consider this case as an example of one of the forms of hermaphroditism it should be classified as pseudohermaphroditismus masculinus.

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SOME HYPOTHESES REGARDING RENAL TUBERCULOSIS¹

ARTHUR L. CHUTE

Before proceeding to the short paper that I have prepared in lieu of a formal address, there are a few remarks that I wish to make. In the first place I thank the Society for the honor they conferred upon me by making me their president: it is an honor that I greatly appreciate.

Since our last meeting momentous changes have come to the whole world. You will agree with me, I am sure, that the Urological Association is to be congratulated upon the part that its members took in the world war. I do not know the proportion of our members who were in service but it must have compared very favorably with that of other societies—it sometimes seemed to me that I was the only one who was not in active service. You know that the urological work of the army, both the direction in Washington and the active supervision in France and in this country were almost entirely under members of this Society. You know also that the work was well done. Not only did our members give their time and the best that was in them in the way of professional skill but one at least, Beal of Worcester, laid down his life. I think we may say that the Society did its part well.

In this post bellum period of discontent which I am sure may be partly, at least, considered as a striving for better things, we have a part to play both as individuals and as a society. As individuals our tasks vary to such a degree as to make any discussion of them unprofitable. We must welcome and help innovations which are real advances and attempt to curb changes which in our opinions are not real advances but are simply the result of the restlessness of the hour.

¹Read at the meeting of the American Urological Association, New York, April, 1920.

As a society I do not see that we have any particular medical reconstruction problems; those of our members who lean to the venereal side may have an increased responsibility put upon them just now because of the relaxation of morals that war is said to bring about. It may be especially incumbent upon them at this time to teach the dangers of venereal infection.

It seems to me as a society that we have certain problems before us, which we should be turning over in our minds. This Society has more than 500 members. At our annual meeting and at the branch meetings a great many papers are read. There is a constantly increasing, and I believe legitimate desire for some publication other than our transactions which shall publish these papers and keep the widely scattered members of this Society in touch with what the members in other parts of the country are doing. I get a great deal of stimulus and inspiration from our meetings but I get it all at a time, that is, at the time of the annual meeting. I believe that many of us feel that a journal of some sort in which this Society has an interest, I will not say exclusive interest, would be of great advantage, and keep a part of our inspiration up during the whole year.

We have in this Society certain conflicts of authority which may be likened to the clashes that we are now witnessing between the federal and state authorities regarding the enforcement of the eighteenth constitutional amendment. I refer to the dual membership that we require of a large proportion of our members: it may seem wise to make some changes as regards this matter.

With 500 members the question comes up whether in the future it will be the part of wisdom to limit membership in this Society to those who have a definite and active interest in urinary work. We have in the past taken many men whose interest in urinary work was passive rather than active: it may be that we shall have to change our policy limiting our membership to a certain extent. I hope, however, that no such action will be taken without it is definitely determined that a change of policy is absolutely necessary.

There is in the country at large, so far as I can learn, an alarming increase in the number of malpractice suits that are being

brought against physicians. This condition is not due, so far as I can determine, to physicians being less careful than heretofore of the interests entrusted to them but to other changes that have taken place in the community as a whole. I feel that our members coming from all parts of the country as they do should take this problem up with their state medical societies and should see if some way can be found to lessen the annoyance, financial loss, and injustice that many of these suits have brought to medical men.

I wish to call the attention of the Society to these matters and to ask them to take them under consideration that they may have their ideas formulated should any of these matters come up for action.

As I understand it, the chairman is allowed more or less latitude in the scope of his address. On this occasion I wish to exercise my prerogative by presenting a paper which perhaps some of you may feel deals more with fancy than with fact.

The question of how infection takes place in renal tuberculosis has for a long time been of great interest to me, but has never been explained to my entire satisfaction. I assume that all will agree that a kidney is never the primary location of a tuberculous invasion but that it always represents an infection that has been transferred from some other focus in the body. The theory that the tuberculous infection comes to a kidney from the thorax by way of the lymphatics has always seemed to me unsatisfying: it, for one thing, offers no satisfactory explanation for those cases where the process is apparently secondary to a tuberculous bone or joint lesion, as is not infrequently the case. The weight of evidence seems to me absolutely against the probability that the infection in renal tuberculosis ascends from the bladder except in very rare instances that are marked exceptions to the general rule. For example one sees patients with a considerably diseased kidney in whom the bladder is little and occasionally not at all involved; a ureter now and again shows definite thickening above with little change below. The careful history of a patient will often elicit evidence suggestive of kidney involvement before the usual bladder distress appeared. If the renal infection had its

origin in a bladder process, one would not expect the bladder process to clear up as it does in a large proportion of cases following the removal of the tuberculous kidney.

To me the most satisfactory explanation of the way in which the infection takes place in renal tuberculosis is to assume that the tubercle bacilli are brought to the kidney by the blood stream. This will account not only for the infections that have their origin in old tuberculous lesions of the thorax or abdomen but also those that apparently come from an old bone lesion that is situated some distance away, and from which there would seem to be no reasonable probability of lymphatic infection.

While this bringing of tubercle bacilli by way of the blood stream from a previously existing tuberculous lesion of the body is the most satisfactory explanation for their entrance into the kidney, certain objections to this present themselves at once. For instance, in other hematogenous infections of the kidney we have found that the infection is almost always bilateral, much more marked on one side than the other, it is true, but none the less plainly bilateral. The proof of this bilateral involvement in hematogenous infections I have demonstrated in certain cases by catheterizing the ureters, and in one instance by the persistence of pus in the urine after the removal of an acutely infected kidney. A few cases, in which neither the ureters have been catheterized nor a kidney removed, have shown evidence suggestive of bilateral infection by the history of the pain which at the onset was sharp in one side but which after a relatively short time became so acute in the other side as to entirely divert attention from the side in which it began. We may say I believe that the presence of bilateral infection has been demonstrated in a sufficient number of cases of hematogenous infection of the non-tuberculous type to make it seem probable that it exists in all or nearly all; it was in fact the recognition of this that led to the protest against nephrectomy as a routine treatment for acute hematogenous, renal infections.

In renal tuberculosis the various series of cases show that the tuberculous lesion is confined to one kidney in most of the cases—in some of my own cases of renal tuberculosis that I went over

a few years ago, I found that only one case in seven showed a bilateral involvement. This fact and another commonly observed fact, namely, that once a kidney has been demonstrated to be tuberculous, it never gets well, at least in the ordinary sense in which we use the term "get well," seem to raise objections to the hematogenous route, as the common way in which infection takes place in renal tuberculosis. If these two observations are correct, namely that in hematogenous infections, the usual course is to have both kidneys infected, and that also when once a kidney is infected with tuberculosis, it is the rule to have the disease progress until that kidney is fully destroyed; if these things are true, we should, provided the infection in renal tuberculosis is by the blood stream, have a great many cases in which renal tuberculosis is double: this we know is not so and would consequently seem to argue against the probability of hematogenous infection.

A few clinical facts that have come under my notice I believe help to reconcile facts that are apparently contradictory, and also allow one to formulate what seems to me certain reasonable working hypotheses regarding the manner in which infection comes about in renal tuberculosis.

These facts which I wish to bring before you briefly, are shown in the appended case histories:

Case I. A man of thirty-seven had several attacks of colicky pain in his right loin—sometimes the pain was very acute indeed, but most of the time it was only grumbling. The urine showed a few leucocytes, and a few red cells—no tubercle bacilli could be found. There was no frequency of urination or other symptoms referred to the bladder. This condition went on for a year or more. Finally a small shadow which moved with the kidney, was found in the right renal region and it was believed that this was the cause of his pain. His right kidney was cut down upon and a calcified area was found in the cortex just under the capsule. This calcified material I scraped away. A small wick was carried down to this point and the loin incision closed about the wick. Within a few days a urinary fistula developed which remained until I removed this kidney some seven months later: at this time it was a typically tuberculous kidney. I believe one is forced to the conclusion that this man had a sub-capsular tuberculous lesion that was healing

slowly and probably would have gone on to definite healing had we not found it, and mistaking its true significance, stirred it up.

Case II. A woman of twenty-seven, whom I saw in consultation in January, 1918, had suffered from pain and discomfort in her left loin for a considerable time. She had been operated upon a week before on the evidence of a radiograph which had shown a shadow in the region of her left kidney, believed to be a renal calculus. When the kidney was exposed, a calcified area was found just under the cortex and this was scraped away. This patient's temperature and pulse went up almost immediately following the operation and when I saw her a week later she seemed to me to have a dissemination of her tuberculosis. At a somewhat later time her left kidney was removed. It proved to be a badly disorganized, tuberculous kidney. The patient continued to fail and died of a disseminated tuberculosis three months after her first operation.

In neither of these patients did we have the symptoms or findings commonly seen in renal tuberculosis nor did the kidneys when exposed have the appearance commonly presented by a tuberculous kidney. I have not the slightest doubt that had these patients not been too skillfully radiographed, the relatively slight disease of these kidneys would not have been recognized, they consequently would not have been operated upon and the process stirred up but they would have probably gone on and stamped out the tuberculous process in their kidneys. It is my belief that conditions like these, or perhaps a little less acute, are very common and that by far the greater number occur without a definite diagnosis being made.

I had under my care a few years ago a young man who had pain in his left renal region—the urine showed a few red cells, also a very few leucocytes. Repeated tests for tubercle bacilli were negative. Repeated X-rays showed nothing. This man was annoyed by this condition of affairs for a year or more, then the pain gradually ceased and the urine cleared up. He was well for some time before I lost sight of him. I believe there is a moderate probability that this man had a tuberculous process in his left kidney which was less marked, however, than in the two reported cases, and which went on to recovery.

Cases like these have much suggestive value to me and they have led me to formulate the following working hypothesis:

That incipient and very mild degrees of renal tuberculosis are probably much more common than we recognize them to be, in much the same way, for instance, as we find anatomical evidence of old tuberculous processes in the apices in many patients who have given no definite symptoms of any such trouble during their lives. If we accept the hematogenous origin of the infection in renal tuberculosis, I believe we must assume that tubercle bacilli are brought in approximately equal numbers to both kidneys; that little cortical tuberculous infections are common and that far from going on to the complete destruction of every kidney that is infected they are probably promptly stamped out in by far the great majority of instances. That the generous blood supply of the kidney allows it to overcome perhaps the greater number of infections while yet they are incipient; that only in a relatively few cases in which one kidney is especially susceptible, perhaps due to some local injury or something of that sort, does the tuberculous process overpower it and progress to the point where it is recognizable through the presence of pus in the urine.

When a process reaches this stage, it is potentially, if not actually, quite advanced, since it has overcome the resistance on the part of the kidney: ordinarily such a condition is quite incapable of cure, in the sense that the process can be brought to a standstill with a kidney that is still capable of functioning to a certain extent; naturally the probability of this process overcoming both kidneys is far less than the probability of its overcoming one; according to my cases the chance of both kidneys being overcome is just one-seventh that of one being overcome.

It is my opinion that some at least of the patients who complain of dull pain in one loin and who present a sterile urine that shows a few blood cells and leucocytes are carrying on a struggle to determine whether a tuberculous infection shall overcome a slightly infected kidney or the kidney stamp out the tuberculous infection.

I believe that this last point has perhaps a practical bearing and that one should insist that a patient who is having occasional attacks of acute pain in one loin, with a urine that shows a little

blood and a few leucocytes, or that a patient who is having dull pain in one loin pretty constantly with the above urine changes, of course assuming that there is no definite cause to explain this pain, should be strongly urged of the importance of rest and building up his resistance, for the reason that he may be dealing with an incipient renal tuberculosis which it is possible to definitely cure by proper care.

I present these views as I believe they explain and reconcile certain definite facts about renal tuberculosis that are apparently more or less contradictory. I especially wish to point out that what I have said is almost wholly of academic interest and is not to be taken as advocating any change in our views of the surgical treatment of renal tuberculosis.

THE STANDARD OF CURE IN GONORRHEA

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The question of a standard of cure in gonorrhoea is a much vexed one. Every urologist has laid down his own standard, has written much, and has denounced or pulled to pieces the standards recommended by everyone else. Moreover the standard of cure is approached from so many varying points of view that the end results are bound to be vastly divergent. From the mass of literature on the subject which has flooded the medical press it would be a matter of very great difficulty to work out a standard which would meet all the various requirements laid down, or even compromise the multitude of views, requirements and desiderata which are pointed out to be so essential. It would also require a sort of superman to discover the patient who would be willing to submit himself to the lengthy and uncomfortable ritual of many of them.

In laying down a standard of cure our aim must be:

1. To satisfy ourselves that the patient is cured.
2. To enable us to reasonably guarantee that he will not suffer any relapse.
3. To protect him from any future sequelae.
4. To assure him that, urogenitally, he is noninfectious.
5. To satisfy ourselves that his urogenital system has returned or is likely to return to normal.
6. To inconvenience the patient as little as possible.
7. To detain him in hospital as short a time as is consistent with a reasonable standard of cure.
8. To lay down a workable standard, the technique of which will not expose the patient to unnecessary risks.

Many standards err on the side of being too low, while others aim so high that the carrying out of the various tests and exami-

nations defeats their own end. As we have already pointed out, the urogenital tract is one with which one cannot take liberties with impunity. The warnings sounded with regard to over-treatment and over-instrumentation therefore apply here, and cannot be too often repeated.

One very much used standard of cure was what was known as "the beer test." After the discharge had stopped, and the urine been clear for a day or two, the patient was instructed to drink several bottles of beer. If he had an obvious relapse he continued treatment, but if nothing happened he was promptly discharged as "cured." A similar test was used in military hospitals. The patient was put on "fatigue duty" for several days, or subjected to the attentions of the physical training instructor for several hours a day. Failing an obvious relapse he was discharge as cured.

Various standards of this mild type have been employed and advocated from time to time. Particularly in military circles, where one hospital vied with another to reduce the "average stay in hospital" to a minimum, the standard of cure was very low. Many workers have put forward claims to rapidity of cure for their methods, but in most cases the standard of cure demanded was never a high one. A few days free of discharge, a clear urine, and a smear gonococci-free were considered sufficient. If the case relapsed, as it did in a very considerable percentage of cases, the soldier went to another hospital, or had moved to another battle zone, and the statistics of the original quick-cure hospital did not suffer. In many cases this seemed to be the goal of their desire.

Too severe standards, however, are equally harmful. Many standards have been used which are practically unattainable, and the result is that the patient carries on month after month suffering miserably all sorts of tests, treatment methods, instrumentations and explorations. In the long run he becomes a confirmed worshipper at the shrine of introspection, a miserable neurasthenic, and an unhappy sexual degenerate. If he is an intelligent man he suffers all the agonies of a proved carrier, whose knowledge of his infectivity sears into his soul. The

"morning drop," the occasional shred in his urine, and possibly the indurated patch in his epididymis all go to make him thoroughly miserable. It is quite common to find such a patient passing urine in the quiet of his own apartments and examining it carefully for shreds, pus or mucus for himself. He lives only for the pathologist's reports, and interprets each finding in his own particular way—often with much originality, inaccuracy and apparent relish. If these reports are not communicated to him, he will cease to be induced to continue treatment, and the standard becomes unworkable, which, possibly, is all to the good.

Various factors have been utilized in compiling an exhaustive and rigid standard of cure. These are of varying value alone and in combination, and will be considered individually. They are: (1) Examination for discharge, (2) examination of urine, (3) behavior after exercise, (4) absence of complications, (5) provocative vaccine, (6) the search for gonococci, (7) the urethroscope, (8) the complement-fixation test, (9) the period kept under observation, (10) subsequent examinations.

1. *Examination for urethral discharge.* So long as there exists a definite urethral discharge, there can be no question of cure. In chronic cases, however, the discharge possibly only exists first thing in the morning, and when the patient comes up for examination there is no apparent discharge. When this occurs, and the patient's statements are unreliable, the greatest care must be exercised not to damage the urethra in any wild attempts to secure some evidence of a meatal discharge. Squeezing the glans and "dripping" the penis from bulb to meatus must *never* be done. If there is no obvious discharge, no stickiness of the meatal lips, and no apparent moisture, one must turn one's attention to other methods of obtaining evidence of progress or cure.

2. *Examination of the urine.* An early morning sample in two glasses is best. Should the urine remain clear for some days, this will form a most valuable guide when combined with other tests in compiling one's standard. Should there be persistent threads in the urine, however, it is most unwise to continue local

treatment indefinitely in an effort to get rid of them. Should this be the only unfavorable sign, and the only requirement of the standard not fulfilled, it is well to cease treatment altogether and discharge the patient. Many men with perfectly healthy urinary tracts go on passing threads in the urine all their lives.

3. *Behavior after exercise.* After all discharge has ceased, and both urine glasses have been clear for several days, the patient should be allowed vigorous exercise for two days, and a careful watch kept for the re-appearance of symptoms. Should no discharge reappear, and the urine show no turbidity and no increase of threads, these points are calculated in his favor. Should an obvious relapse occur, however, further treatment must be instituted.

4. *Absence of complications.* The condition of the seminal vesicles, prostate, vasa deferentia, epididymes, joints and skin should be thoroughly investigated. The urethra should be free of any appreciable infiltration, and all possibility of any active focus eliminated.

5. *Provocative vaccine.* When all possible complications have been excluded, the discharge has ceased for three or four days in spite of exercise, both urine glasses have been persistently clear, the prostate and seminal vesicles have yielded a normal secretion, and all treatment has been stopped for several days, a provocative vaccine should be given. A dose of 100,000,000 stock polyvalent gonococcus vaccine is administered subcutaneously, and the urine examined on the following morning. These examinations are continued for at least a week, and should no relapse occur, there is little likelihood of any serious accident. Should there be any concealed focus of latent gonococci, however, there will be a definite precipitation of symptoms. The urine will become turbid, the discharge may reappear, and on microscopic examination organisms in large numbers may be demonstrated.

This procedure is a most valuable and essential part of any standard of cure. It is efficacious, and unlike "the beer test" cannot be repeated by the patient for his own satisfaction. Moreover, it cannot possibly do the patient any material harm.

6. *The search for gonococci.* Unless there is a very apparent urethral discharge, this search is of little value. Especially in chronic cases organisms may be absent in 99 out of 100 examinations. On the hundredth examination they may appear. It is well known that organisms are often present and cannot be found.

The plan of struggling to eradicate the last gonococcus has led to the mode of over-treatment, which is responsible for converting the urethra into an ideal hunting ground for the gonococcus, so much so that many of these overtreated cases will probably never be cured. We cannot be absolutely certain of exterminating every gonococcus. In spite of the most rigid tests and examinations we cannot guarantee that the last organism has been exterminated. Moreover, it is well known that the gonococcus may lead an indefinite saprophytic existence, and be absolutely non-pathogenic. If then, the gonococcus is non-pathogenic and can do no possible harm, why persist in the effort to exterminate it? Such persistent and prolonged efforts serve only to damage the cells of the host and perpetuate the life of the organisms. In this way the means defeat the end.

When examining prostatic secretion with a view to determining cure, the presence of pus is more important than that of organisms. Leucocytes and pus cells should have disappeared from the prostatic secretion before any idea of cure is entertained. Treatment, however, need not be pushed simply to attain this end within a certain number of days. Rather than risk the damage likely to be caused by overtreatment, one ought to be satisfied if the prostatic and vesicular secretions become normal three or even six months after active treatment has ceased.

There is no certain test for cure, therefore clinical observation is much more important than a perpetual search for organisms, and must form the fundamental basis of any standard of cure.

7. *The urethroscope.* It has been laid down by many authorities that no certain cure can ever be guaranteed until the urethra has been explored from the vesical neck to the meatus several times, and has been found absolutely normal. Indeed it has

been taught energetically, and copied from one text-book to another, that the urethroscopic examination is the most important of all tests of cure.

With this we cannot agree, as routine urethroscopic examination before a patient is discharged from hospital is as unnecessary as it is dangerous. Moreover, treatment has been stopped for so short a time that the urethra has not had chance or opportunity to fully recover. By other methods we have already satisfied ourselves that there is no appreciable infiltration, no area of subresolution, no active infected follicle. What are we likely to gain, then, by learning that the urethra dilates equally and well, that its mucous membrane is recovering its normal color and brilliance? Again, should we find an abnormal urethra—as in most cases we would—a mild general hyperemia, an interference with vascular striation, a certain amount of thickening of the folds, what is our procedure? Are we to continue treatment, or keep the patient in hospital under indefinite observation, or simply discharge him as if he had never been urethroscoped? The first proposal is harmful and likely to do damage, the second is irksome and intolerable to the patient and the third, while possibly the correct course to adopt, shows up the futility of having carried out the examination at all.

Urethroscopic examination may be of value three, or perhaps six months after all treatment has been stopped, and no relapse or complication has occurred. By this time the urethra will have settled down, and a real estimate of its condition may then be obtained. Should everything be well, and the urethra to all intents and purposes be normal, a final pronouncement of cure can be given with tolerable certainty.

When such an examination is made, the following points should be noted:

1. The color of the mucosa should be uniform throughout, and should show a brilliance and glistening appearance which readily reflects light from every point. There should be no hyperemia, and no unequal patches

2. The folds should be numerous, well formed, equal, and sharply-defined.

3. The urethra should respond readily and equally to air dilatation. Should any part respond sluggishly and unequally, subsequent treatment should be instituted.

4. The vascular striae should be well defined and readily visible.

5. The mouths of the glands of Littre and lacunae should be of the same depth of color as the surrounding mucosa. Indeed, they should be scarcely visible. There should be no swellings, no cystic excrescences, no inflammatory rings or color changes.

This picture will usually be found at this time, and the surgeon may give his pronouncement with the utmost confidence. Immediately on cessation of treatment, however, the picture is seldom that of a normal urethra. Indeed the urethra is still suffering from the effects of instrumentation, from the prolonged contact with antiseptics and other chemical agents, and from a prolonged though mild hyperemia. It is therefore extremely difficult and often impossible to give a confident pronouncement.

8. *The complement fixation test.* This test has as its underlying principle the detection of specific antibodies in the serum. To interpret the test successfully one must look upon a strongly positive reaction as indicating an efficient response on the part of healthy tissues, and therefore justifying a favorable prognosis. A weakly positive result would indicate a failure on the part of the tissues to produce sufficient antibodies in response to the specific antigen. A negative result in a serum which has previously been positive, may be looked upon as very strong presumptive evidence of the destruction of the organism.

Experience has shown however, that more accurate information as to the serological types of the gonococcus, together with a more sensitive antigen, will be required before more reliable, sensitive, and specific results can be obtained. It has also been shown that cases of mild anterior urethritis without spread or complication frequently react negatively throughout the attack, and that the more severe the attack and the more extensive the spread of the organism, the more likely is one to get a positive result.

Once the host has had to produce antibody, its manufacture

probably goes on for a length of time after the destruction of the organism. This length of time varies with the duration and activity of the organism. It has been shown that antibodies persist in the serum three months or longer after the organism has been destroyed. So far as the test lends itself to interpretation at the present time, the only criterion of cure which one can lay down is, therefore, a change in the reaction from positive to negative three months after the discharge has disappeared and all treatment has been stopped. The possibility of error lies in the faculty of the gonococcus for lying dormant in some situation walled off from the general circulation so that antigenic substances cannot reach the blood stream. In addition, the artificial immunity produced by vaccine therapy, and particularly by detoxicated vaccines, rules out the complement fixation test as a reliable and useful adjunct to a standard of cure.

9. *The period kept under observation.* It is a very dangerous proceeding to discharge a patient immediately symptoms have cleared up and treatment has been suspended. A period of close observation is most important. This varies from four to twelve days, as a rule. One must insist, however, that four days is too short a time to be of any real value. Twelve days may be considered sufficient. During that time daily examination of urine, discharge, and so on are carried out and the patient allowed considerable exercise. No treatment whatever is undertaken.

10. *Subsequent examinations.* The patient should be required to return in three months' and again in six months' time for further overhaul. On these occasions the test should include (1) examination of urine; (2) massage of the prostate and examination of the secretion; (3) a provocative vaccine if practicable; and (4) urethroscopic examination, chiefly with a view to determining the dilatability of the urethra. Then, and not till then, is the surgeon in a position to give a definite prognostication with any degree of certainty or confidence.

Many standards of cure have been advocated, some combining all the requirements we have just discussed, others employing certain of them only.

The following standard laid down by Simpson and Clarkson is a good example of the rigid type:

1. Suspend treatment for at least one week. Patient should be advised to take alcohol as a provocative stimulant. If for any reason this should be considered inadvisable, the alcohol may be administered as a non-recognizable constituent of some palatable mixture.

2. Patient to present himself for examination, having if possible refrained from micturition all night, or, at least from four to six hours. Meatus examined and urethra "milked up" from bulb. The bacteriologist takes meatal drop on platinum loop, film is made, culture tube is then inoculated. If no meatal drop then platinum loop is to be passed into urethra, and mucous membrane stroked forward, and film made and tube inoculated from wire. Patient micturates first portion of urine into sterilized vessel, which bacteriologist examines in culture media. Centrifugalisation to be carried out or not as seems desirable. Any threads or deposit examined in film and culture. Glans penis is cleansed with soap, and later on with sterilized water, foreskin retracted, and urethra washed out with sterilized water, and patient placed in knee elbow position. The glans penis is not to be touched; shake out last drop of fluid in urethra. Systematically palpate prostate and seminal vesicle, special attention to be made to any feeling of abnormality, e.g., thickened or occluded vesicles or nodules in prostate. Massage prostate and vesicles till a drop appears at meatus or presents itself after milking urethra forward from the bulb.

Films are then made of the prostatic and vesicular fluid and culture tubes inoculated.

Finally a urethral examination should be made, preferably by Wyndham Powell's instrument with magnifying eye-piece. The instrument having been passed, the anterior urethra from the bulb forwards is carefully examined in order to ascertain its condition as regards (a) hard or soft strictures or infiltrations; (b) intraurethral warts; (c) infected follicles; (d) any abnormal congenital condition, e.g. angiomata. At the same time the roof and the floor should be carefully palpated over the urethroscope tube in order that any peri-urethral infiltrations present may be discovered.

The perineum should be examined with a view to discovering the presence of cowperitis, perineal abscess, etc.

These writers go on to explain that no mention has been made of the place of provocative vaccines and the complement fixation

test in connection with testing for the presence of gonococci. They realize the potentialities associated with these methods, but do not at present regard their efficacy as sufficiently proved to justify their inclusion in a routine scheme.

From the foregoing it will be seen that we do not recommend such a scheme in its entirety. It is drastic in that it throws work unnecessarily on the bacteriologist, and re-covers a lot of the ground with which we should have been familiar long before the question of cure came up at all. The urethroscopic examination, also, is ill-timed.

A second example of a standard of cure, illustrating the various ways in which the requirements discussed may be combined, is that employed in the Military Hospital, Chiseldon. Summed up, it is as follows:

1. One week clear without treatment.
2. No morning discharge.
3. First and second urines clear, or at most only a few threads.
4. Urine normal after prostatic massage.
5. Smear after prostatic massage negative to pus cells and gonococci.
6. Negative smears after irrigations with silver nitrate 1:1000, and after two successive bougies.
7. No focal reaction after a provocative dose of 200,000,000 of stock gonococcus vaccine.
8. Urethroscopic appearance normal.

Of premier importance in determining a standard of cure is clinical observation. Subsequent to the disappearance of clinical symptoms, every case should be kept under observation for at least twelve days. If he is an "indoor" patient, he should be detained in hospital for this time. He should be encouraged to take vigorous exercise and subjected to the closest scrutiny thereafter. A provocative vaccine should be given, but such harmful procedures as provocative urethral irrigations of silver nitrate 1:1000 or magnesium chloride 1:500 should not be employed. Prostatic and vesicular massage and examination of the secretion macroscopically and microscopically for pus and leucocytes are carried out, and the urine examined daily. Massage of the urethra over a straight or curved bougie should not

produce pus. Urethroscopy should not be carried out at this stage. Every patient, however, should be encouraged to return for re-survey in three and again in six months' time. His urethra may then be explored with advantage.

Tabulated, a satisfactory, workable, and sufficiently rigid standard of cure reads thus:

1. Disappearance of all clinical symptoms, and the cessation of treatment. Clinical symptoms are taken to have disappeared only after examination of prostate, seminal vesicles, vasa, testes, perineum, after dilatation of the urethra, and after disappearance of meatal discharge and turbidity of urine.

2. Patient is kept under observation for twelve days during which he takes vigorous exercise. He is not encouraged or permitted to take alcohol. If an "outpatient," sexual intercourse, emotional disturbers such as the bioscope, lurid novels etc., and unreasonable excesses of any kind, are forbidden. He should be free of meatal discharge, and urine should be clear in both glasses. If, however, a few threads persist, they should be disregarded.

3. A provocative dose of 100,000,000 gonococcus vaccine should be given about the second or third day after cessation of treatment, and no focal reaction should follow.

4. A curved sound should be passed on the fourth and twelfth days, and the urethra gently massaged on the sound. No pus should appear at the meatus, and subsequent urines should be unaltered.

5. In three months' and again in six months' time the patient should return for re-survey. This should consist of:—

- a. Examination of two urine glasses.
- b. Massage of the prostate and seminal vesicles and examination of the secretion.
- c. Exhaustive general systemic examination.
- d. Examination of the urethra from the vesical neck to the meatus. This may be carried out with an olive diagnostic, a curved sound, or in special cases, by urethroscopic exploration.

Should this examination be in any way doubtful, a provocative vaccine should be given, and future action modified according to the result.

Such a standard does the best both for the patient and for the physician. It primarily cuts out the risk of over-treatment, and thereby removes much of the possibility of perpetuating the life of the gonococcus, of permanently damaging the urethra, and of laying the patient open to the risk of complications both local and metastatic. Moreover it submits the patient to the smallest possible inconvenience and runs little risk of turning him into an introspective neurasthenic. A final opinion of non-infectivity should not be given until the re-survey three or six months later has been carried out. Instructions with regard to his sexual behavior in the interval, therefore, should be rigid.

With very little imagination, it is easy to see how tragic may be the results of too mild or too severe a standard of cure. The advocates of "the most stringent standard known to science" forget the tragedy which may be evolved with this very standard as the mainspring of the plot. So also, the advocates of the mild standards forget. As a result of the former, you get the miserable introspective wreck, broken both in mind and in body, passing his days in the full knowledge that he harbors an unclean and harmful germ, and hoping for the cure which day by day becomes more distant. This is the tragedy of the individual. Resulting from the latter, milder, standard you see the bachelor, months possibly, after his reputed recovery, marrying. The sudden, excessive, and persistent sexual excitement gives the lurking gonococcus its chance, and his disease recurs. Not only that, but his bride contracts the disease. The man, having been assured that he had been cured, naturally blames his wife for having infected him. The wife, well aware of her chastity, scorns the man with the most absolute derision. The curtain is now raised on a domestic tragedy of the first magnitude.

There is little to be said for the superficial and imperfect standard of cure. It perpetrates an injustice to the patient, to his wife, or it maybe to his casual and swiftly changing mistress. It is our duty, therefore, in setting up a standard of cure, to consider not only the patient, but, from a domestic point of view, the wife or the wife to be, and, from a sociological standpoint, the fleeting crowd of harlots, or the amorous though

erstwhile mistress. The latter is as much our immediate concern as is the protection of the matron of virtue.

At the same time, one must not submit the patient to unnecessary risks, otherwise he may be responsible for staging a drama with the tragedy of the individual as its central theme.

The urethra which has been permanently damaged by the process of struggling after the ideal and most stringent standard of cure is obviously a very dangerous asset. It has been converted into an ideal and perfect nidus for the gonococcus and any other organisms that happen to come along. Apart altogether from the eventual risk of vesical, arthritic, and nephritic involvement, is not such an interminable carrier a very real sociological menace? Does *he* not also threaten the virtuous matron or the ubiquitous harlot?

While one must damn the mild and imperfect standards of cure totally, whole heartedly and without reservation or qualification, a word of warning must be sounded with regard to the too rigid standards. No difference in the standard, however, should be made in the case of the married man, the potential bridegroom, or the amorous and erratic bachelor. All should be submitted to the same overhaul, precisely the same clinical standard. In this way one will be able best to look after the interests of the individual, to protect the chaste, innocent, and very often, ignorant matron, and to prevent the wholesale infection of the clandestine but enthusiastic amateur, or the confirmed and ubiquitous prostitute.

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THE GRADUAL WITHDRAWAL OF RESIDUAL URINE FROM THE CHRONICALLY OVERDISTENDED BLADDER

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Patients with chronic retention of the urine may be divided into two groups, those infected early and those uninfected or infected after prolonged retention. The patient whose bladder is infected early seldom allows the urine to be retained long enough to produce a large overdistended bladder, because the early onset of dysuria and frequency demand early medical attention. On the other hand, if the bladder remains uninfected with the prostatic obstruction the accumulation of residual urine is so insidious that it remains undetected until after some exposure or intercurrent illness when complete or almost complete retention occurs. With chronic overdistention of the bladder, particularly in the presence of a superimposed bladder infection, it is not uncommon to find the ureters and renal pelves dilated. In these long neglected cases all conditions are favorable for an easy and dangerous infection of the retained urine.

A statement has been common in textbooks for many years that the man suffering from chronic prostatic obstruction who has routinely catheterized himself, even though he has a chronically infected bladder, is a relatively better risk for surgical operation on the lower urinary tract than the one who, although his bladder is not infected, has a large overdistended bladder and has never been catheterized. It is also almost traditional that there is a great deal of risk connected with the sudden and complete removal of all residual urine in such cases. With the sudden withdrawal of the urine there is a corresponding decrease in intravesical pressure and in the tension on the wall of the bladder. This sudden decrease in pressure permits passive congestion, hemor-

rhage and edema of the mucous membrane of the bladder. If the ureters and renal pelves are dilated they also may be involved in the process. Sudden collapse, anuria and death have not uncommonly followed sudden complete emptying.

The usual recommendation for the relief of such overdistention of the bladder is that a catheter shall be inserted and small amounts of urine withdrawn at intervals of from two to four hours, so that the bladder is emptied in from twenty-four to forty-eight hours. Another method recommended is to empty the bladder completely by catheter and partly to refill it with boracic acid solution. In either of these methods, particularly the latter, there is a more or less sudden relief of intravesical pressure giving opportunity for congestion, edema, and hemorrhage from the mucosa. To refill the bladder with boracic acid solution after it has been emptied appears to have little value, since, if edema and congestion occur, such changes will take place during the actual withdrawal of the urine.

In December, 1920, Van Zwalenberg¹ suggested an ingenious method for the gradual withdrawal of urine from a chronically overdistended bladder, whereby a gradual steady decrease in intravesical pressure was obtained. He reported one case in which the method was used with success. This method has been applied, in the Division of Urology in the Mayo Clinic since January 1, 1921, in all cases of overdistended bladder in which the condition could be detected or even suspected before the passage of a catheter.

METHOD OF APPLICATION

The patient is placed in a hospital and made comfortable in a warm bed. A soft rubber catheter is introduced with all aseptic precautions and fastened in place without permitting the escape of any urine. This procedure is possible except in occasional cases in which the catheter has to be passed on a metal guide. In these cases a minimum loss of urine occurs, usually from 10 cc. to 15 cc. The catheter is then connected to a 6-foot rubber

¹ Van Zwalenburg, C.: Emptying a chronically distended bladder. Description of a simple device. Jour. Am. Med. Assn., 1920, lxxv, 1711-1712.

tube, which at its distal end, is connected with one arm of a Y-glass tube. The other arm of the Y-tube is hooked over the edge of a receptacle hung at the foot of the bed. When all is

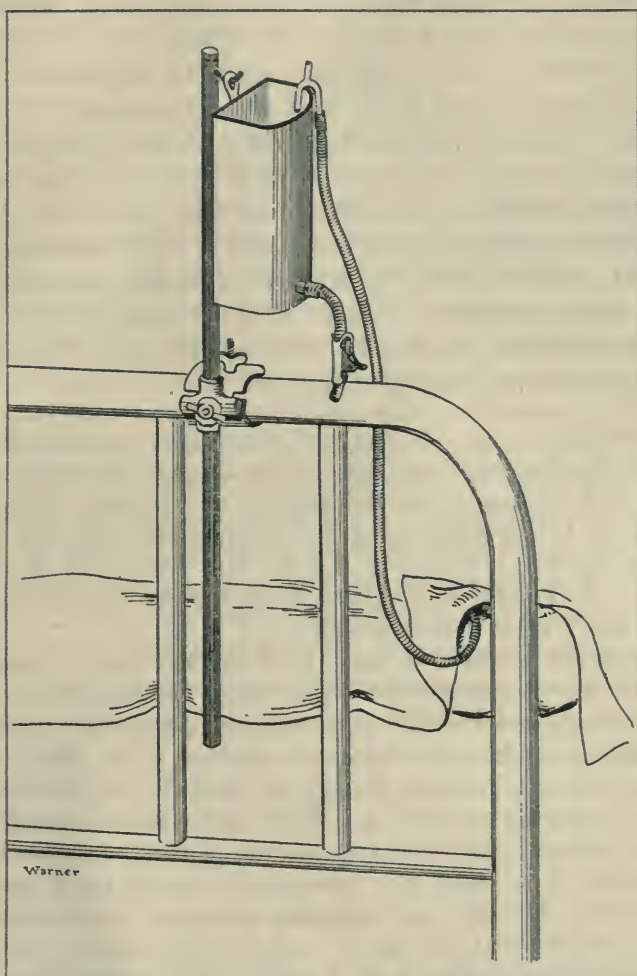


FIG. 1. APPARATUS FOR THE GRADUAL WITHDRAWAL OF RESIDUAL URINE

connected the clamp is removed from the catheter and the height of the urine receptacle is adjusted to a level at which the urine will just trickle over into it on deep inspiration. The tube is clamped

when the patient is fed, bathed, or when any movement is to be undertaken which will disturb the relative level of the bladder and the outlet. An ordinary douche makes a good receptacle, since the accumulated urine may be removed by removing the stopper from the outlet, without disturbing its level. The receptacle is lowered 2.5 cm. each day until the bladder has emptied itself or until the level of the outlet is approximately that of the bladder. When this level is reached the bladder is usually almost, if not quite empty. However, if 200 or 300 cc. of urine remain the intravesical pressure is reduced to nil and there is no danger in completing the emptying of the bladder. The extension tube is removed and the catheter is allowed to remain in place. In one case it was impossible to employ an in-dwelling urethral catheter and the apparatus was applied with a suprapubic drainage tube. The history of this case is as follows:

Case A351,189. Mr. O. A., aged sixty-eight, presented himself at the clinic complaining of inability to pass urine. For eighteen months he had had frequency and difficulty in micturition. Three months before he had been catheterized by his family physician and 56 ounces of urine removed. Following this he had been quite ill. For two months he had had retention with overflow more marked than before. He had lost a great deal in weight.

Examination revealed a large hard nodular carcinomatous prostate. The bladder extended 2.5 cm. above the umbilicus. The systolic blood pressure was 220, and the diastolic was 110. There was no phenolsulphonephthalein return in two hours. The blood urea was 154 mg. and the creatinin 3 mg. for each 100 cc. of blood. An attempt was made to keep an in-dwelling catheter in place but this became impossible the second day. The urethral catheter could not be replaced. The blood urea rose slightly on the third day. A suprapubic stab drainage was instituted under local anesthesia; a rubber catheter was inserted through the canula as the trocar was removed, with a loss of only about 3 cc. of urine. The catheter was attached to the rubber tube just as the urethral catheter had been attached in the other cases. The bladder registered a tension of 25 cm.; it emptied itself in eight days.

After the operation the blood urea rose to 216 mg. and the creatinin fell to 2.7 mg. for each 100 cc. of blood in three days. From this time on gradual and uninterrupted improvement took place. On

the thirty-first day the patient went home still wearing a suprapubic drain, with a blood urea reading of 90 mg., creatinin of 2.5 mg. for each 100 cc. of blood, and a phenolsulphonephthalein return of 10 per cent in two hours. At no time did he have more than 20 red blood cells in a high power field of centrifuged urine.

TYPES OF CASES

Since January 1, 1921, twenty patients have been treated by the method described. The average age of these patients was sixty-six. The oldest was seventy-seven; the youngest was fifty-five. Only two patients gave a history of previous cystitis; two had moderate amounts of pus in the urine. Fourteen patients had definite retention and overflow of from three months to two and a half years duration. Seventeen had not been catheterized since definite retention began. On physical examination all, with one exception, were found to have been in general poor condition. All had distention of the bladder sufficient to cause suprapubic tumor, the smallest extending 6 cm. above the pubis and the largest 2.5 cm. above the umbilicus. In six patients the bladder extended to the level of the umbilicus. Because of the nature of the withdrawal the exact amount of residual urine could not be determined. The phenolsulphonephthalein return was low in all cases. In only three cases was it 15 per cent and above, in three 10 per cent, and in thirteen cases it was nil, or a trace in two hours and fifteen minutes. The blood urea varied between 28 mg. and 312 mg., the average being 81.4 mg. for each 100 cc. of blood. The creatinin was estimated in eleven cases only. The highest creatinin estimation was 6 mg., the lowest was 1.5 mg., and the average 2.4 mg. for each 100 cc. of blood.

RESULTS

The intravesical tension varied greatly; the highest was sufficient to raise a column of urine 27.5 cm. above the bladder level, the lowest was 10 cm., and the average was 14.8 cm. Most of the patients had a tension approximating the average. The rate at which the bladder emptied itself showed an equally wide range of variation and did not always bear a definite relationship to the

tension. It took from two to eight days to empty the bladder; the average time was 4.3 days. The bladder which registered the highest tension, 27.5 cm., emptied at the end of four days, at which time it still had a tension elevation of 17.5 cm. Another case in which the bladder tension was 25 cm. required eight days to empty. In two cases there was urine in the bladder when the pressure was reduced to nil. In three cases hemorrhage apparently due to trauma in the prostatic urethra was appreciable; in each case it followed difficulty with the in-dwelling catheter, and ceased immediately the catheter was removed.

Relative amount of bleeding before and after the application of the apparatus

RED BLOOD CELLS IN A HIGH POWER FIELD OF CENTRIFUGED URINE	PATIENTS BEFORE*	PATIENTS AFTER
0	5	2
1-20	7	7
21-50	2	9
51-100	1	2

* In five cases no record was obtained because of difficulty in collecting the urine.

Eight patients had primary prostatectomy. Two had suprapubic drainage and subsequent prostatectomy. In one of these a two-stage operation was necessary because of the presence of a large vesical calculus. Four others had suprapubic drainage; one of these died after the operation. He had progressed satisfactorily for four weeks up to the time of operation, and death was in no way associated with the removal of the urine. One of these patients is awaiting secondary prostatectomy. One patient who had suprapubic drainage, and four who had in-dwelling catheters, had carcinoma of the prostate. These all progressed satisfactorily and have returned to their homes. One patient with benign hypertrophy of the prostate is at home for the summer and will return in the autumn for the secondary prostatectomy. One patient with carcinoma and recent suprapubic drainage is still in the hospital.

CONCLUSIONS

The method of withdrawing the urine in chronically overdistended bladders is simple, and can be accomplished either with the in-dwelling urethral catheter or with suprapubic stab drainage. This obviates the usual danger associated with the sudden complete withdrawal of residual urine from an overdistended bladder.

A VISIT TO SOME OF THE EUROPEAN UROLOGICAL CLINICS¹

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The hospitals and the one large medical school of Paris have just begun to resume their prewar activity. The majority of medical men of all ranks and specialties were in military service for nearly five years. For the graduate, Paris will prove somewhat of a disappointment if he desires to take intensive courses of a few weeks duration. Although there are many clinics where one is most cordially received, the courses of instruction are arranged primarily for the undergraduate. There is no central office of information where one can find a bulletin of the operations to be performed upon the following day, as is the case in our larger cities. Unless one has secured advance information through a friend, quite a little time is wasted until one becomes acquainted with the location and hours of the various clinics. This is perhaps less true of urology than in any other fields. The two principal urological clinics here are those of Legueu at the Hôpital Necker and that of Marion at the Hôpital Lariboisière. If one desires to see a large number of operations, I believe that the clinic of Marion offers more than that of Legueu. The former operates from four to six urological cases every Wednesday and Saturday at ten o'clock. At Legueu's clinic, the out-patient department far excels that of Marion and one can attend courses of instruction in diseases of the lower urinary tract as well as in the biochemistry, pathology and bacteriology of the genitourinary tract. The courses in urethroscopy, cystoscopy, etc. are given to classes of twelve to fourteen which is quite a disadvantage.

¹The first letter is a report of visits to Marion's clinic at Paris.

This first communication will be devoted to my observations at a number of Marion's clinics. I have attempted to be a fair minded reporter and omitted many details which are familiar to every one of the Fellows of the Association.

Marion is an indefatigable worker and extremely modest. Like many other operators here, he prepares the operative field, arranges the linen, selects his instruments throughout the operation from an adjacent table, sutures every wound himself and applies the final dressing. Much of the operator's energy must be expended unnecessarily as compared to our own methods. Marion has a marvelous memory and will send for monographs and museum specimens illustrating rare cases, both of which he will demonstrate to elaborate his talk upon the material secured at operation, after completion of the latter. He has a well arranged museum and every specimen is turned over to a competent pathologist for detailed study.

One rather interesting feature is that nearly all of the prominent urologists here have had a most thorough training in general surgery and it is not unusual to see a gynecological operation skillfully performed at the same sitting with one for incontinence of urine as in one of the cases to be described later.

Case 1. Subacute gonorrheal infection of a supernumerary urethra.

This was the third case of double urethra which Marion had observed and at the close of the operation, he sent to the museum for the specimens of the supernumerary urethrae which had been removed from his two other cases. The urethral canals in the latter were about 3 inches in length and had the calibre and appearance of a normal pendulous urethra.

In the case which was operated at the first of the clinics reported here, there was a history of gonorrheal infection of the true urethral canal of some weeks duration which had responded to treatment in a satisfactory manner. On the dorsum of the penis was a slightly reddened, firm elevation directly in the midline resembling an inflamed dorsal lymph vessel. At its distal end, that is just above the true external meatus, however, was an orifice from which pus escaped and one could squeeze out similar material by pressure along the dorsum of the penis as far back as the pubes where the swelling ended.

Through an incision along the midline of the dorsum of the penis,

a cord-like mass was enucleated and demonstrated to have a lumen throughout, which ended blindly in its proximal portion, just above the pubic symphysis. It was lined by a mucus membrane exactly like that of the urethra and had a wall about the thickness of the pendulous portion of the latter. Marion, after demonstrating the specimens from two analagous cases, referred to an article on the subject of double urethrae published in an early volume of the *Journal d'Urologie*, from which he quoted. Such a supernumerary urethral canal may end blindly or be open at either its proximal or distal end. If the latter is open it is subject to the same infections (as in the case just operated upon) as the true urethra. It may have a proximal orifice situated just above the internal meatus which can be recognized cystoscopically. Usually the accessory or second urethra is superimposed upon the true one.

Case 2. Intrarenal (true) and extraureteral (false) shadows.

A woman of twenty-eight complained of pain over the right kidney with hematuria. The radiograph revealed a triangular shadow of uniform density opposite the transverse process of the first lumbar vertebra which one could readily interpret as due to a calculus lying at the ureteropelvic junction. A little lower down apparently in the course of the lumbar ureter was a second round shadow of not quite uniform density.

A thorough urologic study of the case had unfortunately not been made. Marion felt quite sure that the two shadows were intrarenal, so that a ureteropyelogram and the use of a shadowgraph catheter had been considered unnecessary. Upon exposure of the lumbar ureter, the lower of the two shadows was found to be due to a caseated, partly calcified retroperitoneal lymph node lying very close to the ureter. The upper of the two shadows was caused by a typical nose-shaped calculus at the ureteropelvic junction, which was removed by pyelotomy. Without further evidence of a renal tuberculosis than the presence of the above described lymph node, he bisected the kidney with negative results so far as confirmation of the suspicion of a renal tuberculosis was concerned. One could not have been more forcibly impressed with the unsatisfactory method of making such a diagnosis at the operating table in an early stage of renal tuberculosis. In spite of a number of deep sutures, the bleeding from the parenchyma continued in an alarming manner and large clots and liquid blood escaped from a tube inserted as one employs it in nephrotomy.

I have given a description of the above to illustrate how difficult it is first, to form a judgment of the organization of a clinic and of the ability of its chief, from a single case, and second, that as one's own experience increases, there is a tendency to be more and more charitable towards what might be considered errors of technic and judgment on the part of others. The case was also very instructive in demonstrating the necessity of a thorough study of every urologic case lest some unusual combination of shadows might exist.

Case 3. Incontinence of urine in adult female.

In a thirty-year old woman Marion demonstrated a new operation for incontinence of urine in the female, due to weakness of the sphincter. He aims to tighten the posterior portion of the neck of the bladder. A Pezzar catheter having been inserted into the bladder, an incision is made (fig. 1) through the vaginal wall (which has been stretched by traction with a vulsellum upon the cervix) 1 cm. behind the external

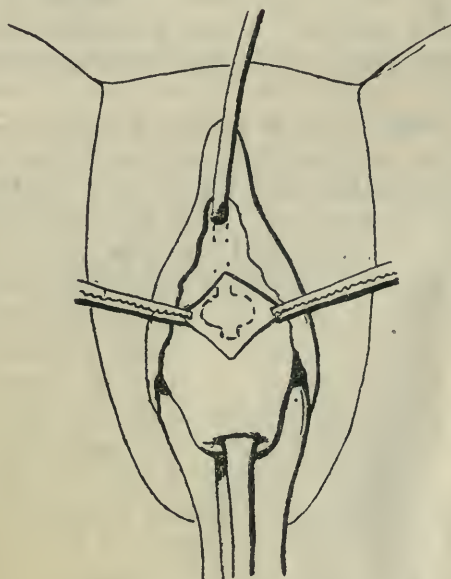


FIG. 1. CERVIX PULLED DOWN AND PEZZAR CATHETER INSERTED INTO BLADDER
Incision made to expose neck of bladder

meatus. The posterior portion of the neck of the bladder is mobilized and two mattress sutures (fig. 2) passed through the tissues at the neck of bladder. After tying this first layer of sutures, they are buried by a second row more superficially placed. After tying this second tier the incision in the vaginal wall is closed. If a prolapse of the uterus

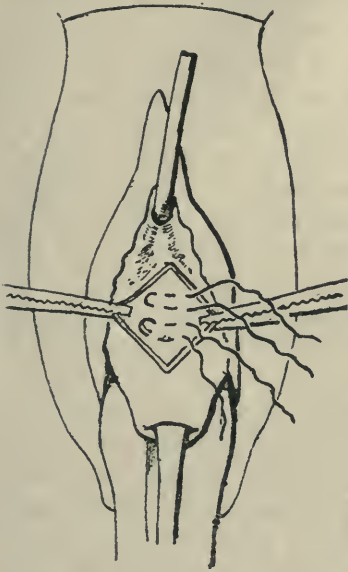


FIG. 2

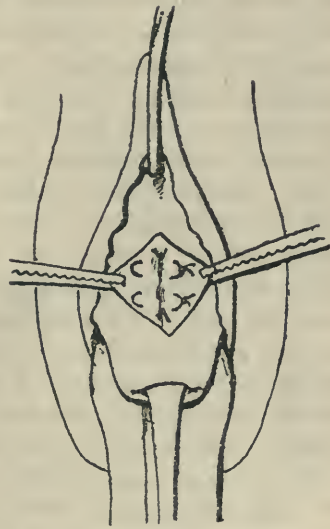


FIG. 3

FIG. 2. MATTRESS SUTURES INSERTED TO NARROW OR REINFORCE MUSCULATURE OF NECK OF BLADDER

FIG. 3. SUTURES SHOWN IN FIGURE 2 TIED
Incision in vaginal mucosa ready to be approximated

complicates the incontinence, a plastic vaginal repair is added. The object of the operation is to narrow the urethra and neck of the bladder in a more effective manner than can be done by the Gersuny method.

One of his assistants recently reported a number of very successful results from Marion's clinic.

Case 4. Resection of large bladder diverticulum, complicated by stenosis of vesical end of ureter of same side, hydroureter and atrophy of kidney with hydronephrosis.

This case was one of the most instructive I have seen since visiting European clinics. A man of forty had been admitted on account of urinary retention which was found after an elimination of other causes, to be due to very large diverticulum. Its opening was low down on the left lateral wall. Before operating, Marion demonstrated a beautiful cystogram showing the shadow due to the diverticulum, which was almost as large as that of the bladder itself. Ureteral catheterization revealed a left kidney whose output of urea was much less than that of the opposite side. The cause of this difference had not been ascertained before operation but was disclosed during the course of the removal of the diverticulum. Upon opening the bladder the orifice of the diverticulum was seen to be about the size of a silver dollar. Upon mobilizing the bladder, the diverticulum was found to be as large as two adult fists. The orifice of the left ureter was sought for, transversically, in vain. In order to remove the diverticulum, an incision was made at right angles to the original bladder incision, directly into the edge of the diverticulum and the latter then invaginated and excised after separating it, with great difficulty, from the structures on the left side and floor of the true pelvis. During this enucleation of the diverticulum, the left ureter was exposed and accidentally divided. This ureter was of the calibre of a small intestine with very thin walls and ended below in a tapering manner similar to the cases of congenital stenosis of the ureter which I have described several years ago. This enormous dilated ureter continued of about the same calibre up to the kidney. The pelvis and main calyces of the latter showed a moderate degree of dilatation. The kidney itself was extremely small, and the narrow rim of parenchyma accounted for the small output of urea on this side. The relations of the greatly dilated ureter to the large congenital diverticulum were so intimate that one can readily understand why it was unavoidable to separate the two. This simultaneous presence of two congenital malformations on the same side and their close relation to each other was a most instructive feature. Marion emphasized an axiom which he usually tries to follow, that is, in the presence of concomitant kidney (or ureter) and bladder lesions, it is better judgment to complete the work on the upper urinary tract first. He studies kidney function by leaving the ureteral catheter *in situ* for two hours, during which time the patient drinks water freely. He then determines in addition to the amount of phthalein excreted during the two hours, the percentage of urea and chlorides excreted on each side as well as the comparison of the results of a microscopic examination of the separate urines.

A nephroureterectomy was performed and then the bladder reconstructed at the point of resection of the diverticulum. I was pleased to be informed at a subsequent visit that the patient's convalescence had been uneventful. The orifice of the ureter had evidently been very close to the edge of the diverticulum.

After demonstrating the removed kidney, ureter and bladder diverticulum Marion sent to his museum for four specimens from similar cases, both operative and autopsy. In one of the latter, it was of interest to note that the ureteral orifice of the corresponding side was within one-fourth inch from the margin of the opening of the diverticulum. After seeing these specimens and thinking of the case just operated upon, I determined in future to leave a catheter *in situ* during the removal of a large diverticulum and also to add a ureteropyelogram of the same side to the cystogram of the case. The sac of the diverticulum was three inches in diameter but could be easily inverted into the bladder after the many dense adhesions had been freed.

Cases 5 and 6. Second step of suprapubic prostatectomy.

The technic in both cases was identical. In one case the first step had been performed ten days before while in the second, the interval was four weeks. In determining the time for the second step Marion is governed principally by the results of the determination of the amount of urea-nitrogen in the blood and by the Ambard constant. He has an open mind in regard to the latter but is not as enthusiastic about it as at the Legueu clinic. Marion is also giving phthalein a thorough trial at present.

As a preliminary measure I was very much surprised to learn that a ligation and division of the vas deferens on each side is done as a prophylactic routine measure against an epididymitis.

Emphasis is also laid upon the advisability of making the opening at the first operation at as high a point in the bladder as possible, usually two fingers breadth above the pubis when the bladder is filled before making the skin incision. In the second step—the opening into the bladder is enlarged with the scalpel sufficiently to admit two fingers and the gloved hand inserted into the rectum, thus enabling the prostate to be supported while being enucleated from above. Marion always examines carefully both the field of operation afterwards as well as the specimen itself and demonstrated in one of the cases that it was very easy in a large prostate to leave *in situ* a fragment large enough to form the nucleus of a recurrence.

Hemorrhage from the prostatic bed is controlled by iodoform gauze,

the end of which is attached to a silk thread so that the latter can be pulled through one of his special large rubber tubes, so that the bladder can be tightly closed around the latter. After placing the gauze the bladder is irrigated with 1:2000 nitrate of silver solution until the fluid returns clear. Marion like Walker of London has great faith in the hemostatic action of such solutions. The packing is not removed until the fourth day. The most important causes of a post-operative fistula is found in his clinic, to be an incision in the bladder which has been placed so low that it lies behind the pubes when it attempts to close. Other causes of fistulae following suprapubic prostatectomy which are less important are too long an incision, separation of the recti, local infection and poor general condition. Stricture of the urethra is exceptionally infrequent in his clinic, as a cause. Postoperative epididymitis is very rare if preliminary ligation is done as I have described above.

Case 7. Renal tuberculosis.

The only features of interest were (a) the division with cautery of the ureter (between two ligatures) close to the kidney, (b) the thorough removal of all perineal fat, and (c) the drainage of the wound with a large rubber tube. No effort is made to remove the ureter or attach it into the incision.

Case 8. Carcinoma of base of bladder.

Although his methods do not agree in many respects with our own, I am simply reporting this clinic with as few criticisms and comparisons as possible.

In the present case, the neoplasm was about the size of a half dollar, ulcerated and sharply demarcated, located at the trigone. Before beginning the removal of the tumor, Marion expressed his preference for complete cystectomy in all cancers of the bladder with double nephrostomy by his method to permit escape of urine from each side. As a rule the patient will not consent to this so he is obliged to do a partial resection followed by radium in the majority of cases. In the case which I saw, he made an incision with a scalpel through the entire thickness of the trigone, three-fourths of an inch from the edge of the tumor.

He usually fulgurates the edges of the excised area and its bed but he failed to do so in this case. He seemed rather skeptical about the ultimate benefit from the use of fulguration or of radium in bladder cancer.

In closing I wish to thank a former assistant of Dr. Misrachi for valuable assistance in interpreting many of the sentences of Professor Marion who speaks so rapidly that it is difficult to follow him without losing many important points. I trust that at least some of the observations will be of interest to Fellows of the Association and will write later about the Legueu and other clinics.

NEW GROWTHS DEVELOPING IN UNDESCENDED TESTICLES¹

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The idea that undescended testicles are prone to develop malignant tumors is old. The condition has recently been observed by the writer for the first time. On account of the rarity of this condition and the features of surgical judgment connected with it leads to the presentation of this matter for consideration and discussion.

The patient who brought this matter to the writer's attention is a man thirty years old who had no congenital defects other than bilateral undescended testes, and whose condition other than this defect was normal in every way. He was operated upon by Dr. Fred B. Lund at the Boston City Hospital on April 27, 1914, for this condition; at which time the right testicle was found to be in the right inguinal canal, associated with a congenital hernia. Nothing unusual was noted in regard to the condition of the testicle and it was placed in the scrotum and the hernia repaired after the method of Bassini. There existed a congenital hernia on the left side and the testicle, regarding which nothing unusual was observed, was found inside the internal abdominal ring. The testicle was placed in the scrotum and the hernia also repaired after the method of Bassini. The patient made an uneventful recovery and left the hospital in fourteen days. The patient remained well in every respect, except for a gonorrhoea in 1917, mild in character, without complications, and from which he recovered in a few weeks. About the middle of May 1919 (five years after the operation for undescended testicles) he noticed that the right testicle was slightly swollen and painful.

He consulted the writer on June 5, 1919 and stated that during the past two weeks that the right testicle had grown rapidly in size. Upon examination it was found that there was a solid tumor in the right scrotum the size of an orange, slightly irregular in contour, with the

¹ Read at the meeting of the American Association of Genito-Urinary Surgeons, Rochester, Minn., May, 1920.

suggestion of a small amount of fluid in the tunica vaginalis. The testicle on the left side was in normal position and was normal by palpation. Both hernia wounds were solid; there was no evidence of the extension of the growth above the scrotum; there were no inguinal nodes palpable, and the prostate and vesicles were normal by palpation and their secretion showed nothing of a pathological character. The patient's general condition was excellent.

Operation, June 7, 1919. The tumor mass was removed, from a scrotal incision which extended up the inguinal canal, without opening the tunica vaginalis. The cord was somewhat difficult to isolate from the scar tissue in the inguinal canal, but the cord was normal in character. The patient made an uneventful recovery following the operation and left the hospital in eight days. The pathological report is as follows:

"Specimen consists of testicle—laid open—occupied by a new growth forming a mass 7 by 4.5 by 4 cm.—Central portion of tumor is soft, rather papillary in character, 3 cm. in diameter, enclosed within a thin membrane. In peripheral portion tumor is lobulated, solid, with small cystic areas. Throughout the mass, especially in peripheral portion, occur spicules of bone.

"Microscopic examination shows a mixed tumor made up of connective tissue, supporting in places nests of atypical squamous epithelium, in places masses of atypical glands, elsewhere bits of cartilage, hairfollicles, and sebaceous glands. *Diagnosis:* Teratoma of testicle."

The patient has been seen lately (eleven months following orchidec-tomy) is in excellent health, and nothing abnormal can be detected.

A perusal of the literature shows that new growths developing in undescended testicles is in reality of rare occurrence, usually occurs when the organ is retained within the inguinal canal or abdomen and the case here cited is the only one that can be found in which a tumor has developed in an undescended testicle, which has been replaced in the scrotum by operation. Buckley, in a most complete and excellent article upon this subject, records fifty-seven cases of new growth developing in undescended testicles collected from the literature up to 1913 and adds two which he had observed, making a series of 59 cases.

I have made a careful search of the literature since Buckley's publication in 1913, and have found one case recorded by Ochs-

ner, one by Butt, one by Grant, all of which were intra-abdominal tumors; and one inguinal tumor recorded by Lister and one instance of bilateral inguinal new growth recorded by Smith. My case, which is unique, had one undescended testicle in the right inguinal canal and the other in the abdomen; the testicle located in the inguinal canal being the one which developed the new growth five years after being placed in the scrotum by operation, while the one placed in the scrotum from the abdomen is apparently normal.

Bringing the reported cases to date we have 62 instances of intra-abdominal tumors developing in undescended testicles and 3 of tumors developing in testicles retained in the inguinal canal, 1 case being unilateral, 1 bilateral, and 1 developing a new growth five years after an apparently normal testicle was replaced in the scrotum.

In this series of 65 instances of new growth developing in undescended testicles 43 were single and 22 double crypt-orchids. There are 34 instances of the growth developing on the right side, 25 on the left, and 3 bilateral. There are 3 instances in which the side affected is not noted.

Regarding the feature of *age* in connection with the subject it is found that tumors developing in undescended testicles is similar to tumors developing in normally placed organs; that is in adult life during the period of greatest sexual activity. The youngest patient in the series here recorded is seventeen years of age and the great majority are between the ages of twenty-five and forty so that there seems to be nothing in the condition of undescended testicle per se favoring an earlier development of new growth.

Of the *side involved* this point has been determined in 62 of the 65 patients. The right side in 34, the left side in 25, and bilateral in 3. In 4 of the series there were sexual characteristics that made the sex questionable, 2 being classed as males and 2 as females. (Male cases, Primrose, Marchand; female cases, Marion, Abel.)

The *prognosis* as in all malignant testicular tumors is bad, and the *mortality* is high. The majority of the patients in this recorded series were dead within one year following operation and

Buckley states that only 3 of the 59 patients which he recorded were alive after two years.

Hinnman has pointed out that metastasis from a malignant tumor of the testicle may always be expected to take place in the lumbar lymph nodes, particularly in the nodes in the region of the renal pedicle when the tumor is on the right side and to the left of the aorta when the growth is located in the left testicle. Hinnman had advocated the removal of these nodes in connection with orchidectomy when these nodes are not clinically involved; basing this opinion upon the fact that but 15 to 20 per cent of patients with testicular new growth are cured by orchidectomy even before metastasis have taken place.

The classification of tumors of the testicle has not been uniform. In the series here presented the growths have been described as sarcoma of different varieties, carcinoma, cancer, epithelioma, rhabdomyoma and teratoma. Erving's classification, including all testicular new growths into one class of teratome or derivatives, is now generally accepted from the clinical viewpoint, and of two types, simple or complex teratoma or round-cell embryonic carcinoma. All testicular new growths may be considered malignant, and it is a well recognized fact, from the pathological viewpoint, that in the testicle more than any other organ it is possible to maintain a single embryonic origin of the great majority of tumors.

It is of interest to compare the relative frequency of new growth developing in the testicles normally placed, and those abnormally located. Eccles found in 38 cases of sarcoma of the testicles but 1 in an imperfectly descended organ. Howard, in 57 cases found 48 in testicles normally located and 9 in ectopic testicles. Bulkley, in 11 testicular tumors records 9 as scrotal tumors and 2 as malignant abdominal tumors of testicular origin. Chevassu records a relative series of 113 scrotal testicular tumors to 5 abdominal testicular tumors. Odiorne and Simmons found 48 scrotal tumors to 4 abdominal tumors of testicular origin. Hinnman, in a study of 32 patients found 7 to be in undescended testicles. Coley (discussion of paper by Grant) states that in 64 cases of new growth of the testicle 12 occurred in undescended testicles.

I have found 67 tumors of the testicle at the Boston City Hospital in which a histological diagnosis was made, all of which were testicular tumors originating in organs located in the scrotum and there were no tumors of testicles improperly descended. A *summary of these figures* shows that of 452 tumors of the testicle, 412 were developed in organs normally located and 40 in organs imperfect in their descent, which figures show that new growths occur 10.3 times more frequently in testicle normally descended than when imperfectly descended.

It is generally believed, upon what ground I am unable to ascertain, that undescended testicles lack the power of spermatogenesis and that transplantation into the scrotum does not change this feature. Eccles, however, asserts a contrary view. Whatever the truth of this matter may be the important point is whether or not transplantation has any influence upon potential malignancy. This is suggested by the fact that there has been but one patient observed who has developed malignancy in a retained organ transplanted into the scrotum and as we realize, the operation for undescended testicles is common. From the series of testicular new growth here recorded, and in the consideration of the whole subject of tumors of the testicle, it is noted that malignancy of the testicle does not manifest itself before the age of puberty, and it is an accepted fact that testicles imperfectly descended may make their way into the scrotum any time up to the age of puberty, which argues against operative interference before that time, unless an associated congenital hernia possesses features demanding it.

After the age of puberty a descent of retained testicles is not to be expected, and it has been shown that it is during the years of sexual activity that malignancy in the testicles manifests itself. For that reason it would seem good judgment to deal surgically with the abnormality of undescended testicles soon after the age of puberty; placing the imperfectly descended organ or organs into the scrotum when possible, and removing such organs when technical difficulties make this impossible. The rarity of new growth in testicles placed in the scrotum has been shown; the tendency to malignancy should be considered a constant factor in all tes-

ticles after the age of puberty, as noted by the relative frequency of such disease in normally descended organs; and, moreover, if new growth is going to develop in an imperfectly descended organ placed in the scrotum by operation the condition is more readily noted and can receive earlier treatment than if the testicular new growth develops in an organ retained in the inguinal canal or abdomen.

DISCUSSION

Dr. E. L. KEYES, JR., New York, N Y.: I have had the good fortune to operate upon a good number of cryptorchids because men are sent from the fire and police departments to Bellevue Hospital for operation. I have done and have had done in my service operations on about 40 patients, and that means a much larger number of testicles. These were all in young adults, and we did not find evidence of teratoma in any of these cases.

During my practice I have seen three cases of malignant growth of abdominal testicles. One of them was reported in the literature as a sarcoma of the prostate, which was undoubtedly a teratoma of an indwelling testicle.

As to the point Dr. Cunningham brought up about not operating upon these cases until they reach maturity, so that any growth present may be found, I think delaying operation until maturity might impair the spermatogenetic function more than if the operation is done earlier. My own impression has always been to operate as soon as the patient is about eight years of age, and the structures are definite and large enough to encourage the prospect of being able to save the testicle.

Dr. CUNNINGHAM (closing the discussion): I have only a word to say in answer to Dr. Keyes. I think it is better, if possible, to delay operation in these cases until the age of puberty, hoping for a descent of the organ. I do not think operation at that time would impair the spermatogenetic function, and it seems safe, as regards the development of new growth, to wait until the age of puberty as new growths in retained organs have never been found before the testicle develops the function of spermatogenesis.

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A CASE OF TRUE LATERAL HERMAPHRODITISM IN A PIG WITH FUNCTIONAL OVARY¹

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That variety of true hermaphroditism which is characterized by the presence of an ovary on one side and a testis on the opposite side is one of the rarest forms of structural abnormality of the genitalia. No undoubted cases have yet been reported in man, and but two instances have been observed in swine. Some idea of the rarity of the condition may be gained from the results of a systematic examination of 500,000 swine made in the Berlin municipal abattoir, under the direction of Ludwig Pick (1914). In this series of animals five cases of hermaphroditism were observed, but none of them was of the lateral variety, a mixed gland (ovotestis) on one or both sides being present in each.

Reuter (1885) described the case of a two months' old pig, discovered among a litter which also contained two pseudo-hermaphrodites. This animal possessed a right testis and a left ovary. The ovary was very small but contained ova in primordial follicles; the testis contained numerous interstitial cells, but apparently there were no germ-cells in the tubules. On the side on which the testis was located the uterus ended in a rudimentary Fallopian tube.

Kingsbury (1909) recorded the examination of a young adult pig with male external genitalia. There was a normal-looking uterus with a rudimentary left ovary and a large right testis with a typical epididymis. On the right side the Fallopian tube ended in a diminutive blind sac. The ovary contained a few ova in follicles; the testis had the typical structure of a cryptorchid

¹ Reprinted from Publication 274 of the Carnegie Institution of Washington. Since the preparation of this paper a similar case has been described by P. Ancel, *Comptes Rend. Soc. Biol. Paris*, lxxiii, 1642-1644.

testis, with numerous interstitial cells but without germ-cells in the tubules.

DESCRIPTION OF SPECIMEN

The author's specimen, consisting of the uterus, tubes, and ovaries of an adult pig, was found among a number of uteri which had been brought in from a neighboring slaughter-house for study; therefore no information is at hand concerning the history or appearance of the animal from which it came.

The uterus was normally formed (fig. 1), presenting two cornua as usual. Its size corresponded to that of the uterus of a young, sexually mature sow. On the left side the uterine cornu ended in a normal Fallopian tube in connection with a normal ovary; the latter contained four recent corpora lutea, one of them cystically dilated. On washing out the contents of the tube with saline solution, one ovum was found, normal in all respects except that the cytoplasm was slightly shrunken; one polar body had been extruded. The right uterine horn, normal in size and form, ended in a very slender tube about 1 mm. in external diameter near the uterus, which gradually thinned down to an almost linear dimension, losing its lumen, and finally ending in the connective tissue over the epididymis (fig. 1).

On the right side, in place of an ovary there was a mass 30 by 25 by 20 mm. in diameter, of dull flesh-color, exactly resembling a testis in form, texture, and color. It was covered by a thick capsule in which large and somewhat tortuous vessels coursed; when this tunic was incised the contents bulged over the cut edges. The exposed surface was dry and granular in appearance.

On this side of the uterus there was a well-defined Wolffian duct, such as is occasionally present in sows, beginning in the vagina and running parallel to the uterine horn between the layers of the broad ligament. However, instead of ending in a cul-de-sac or in a series of minute cysts in the region of the ovarian pedicle, as this duct usually does when present in the sow, it became greatly convoluted as it approached the tip of the cornu and finally so closely coiled as to form the body indicated in figure 1. This structure presented the appearance of an epididymis by

reason of its texture, its close apposition to the testis-like body, and also because of a slight constriction at the middle portion, suggesting a division into globus major and minor.

Microscopic examination fully confirmed the foregoing interpretation and proved that the specimen was indeed one of true lateral hermaphroditism. Sections of the testis (figs. 2 and 3) showed a typical tunica albuginea, within which the gland substance consisted of tubules separated by relatively wide groups of interstitial cells of normal appearance, in whose nuclei mitotic figures were occasionally found. The tubules were lined by a layer of high cells, nowhere more than one cell deep, except that here and there a nucleus lay farther from the basal margin than the others. The nuclei were of medium size and contained relatively less chromatin than those of the interstitial cells. No mitoses could be found. The cytoplasm toward the free border was frayed out into long irregular strands which were so interlaced that the lumina of the tubules seemed in most places to be filled by this vague network of protoplasmic material. Within the cell-bodies of this epithelial lining there were numerous large vacuoles. Germ-cells were totally lacking; no tubule contained any cells other than those already described, which were presumably partially degenerated Sertoli cells. The connective tissue of the testis was normal in appearance, showing no sign of the hyaline degeneration which has sometimes been seen in hermaphrodite glands. The epididymis (fig. 4) was similar in all respects to that of a normal male animal except that it contained no spermatozoa.

In order to gain a general view of the ovary it was cut into six blocks and sections were taken from each of these portions; these presented everywhere the histological structure of a normally functioning organ (fig. 5). The corpora lutea were recently formed, with the membrana propria broken down and the elements of the theca interna just beginning to invade the granulosa, indicating that ovulation had taken place about three days before. (For grounds for this estimate, see Corner, 1919.) This finding is of course in accord with the presence of an ovum in the tube. No special significance is attached to the fact that one of the

corpora lutea was slightly cystic, since this is a common occurrence in normal swine. The cortex of the ovary contained primordial ova and there were numerous follicles of normal type. Due consideration was given to the possibility that small masses of testicular tissue might be present in the ovary; that is, that the organ might be an ovotestis (as in one of Pick's cases, which macroscopically closely resembles ours), but no foreign tissue was found.

The uterine mucosa was normal and similar in both horns. From the results of studies on the cyclic changes in the uterine mucosa, now in preparation, the author feels justified in stating that the uterus of this animal presented the microscopic features characteristic of the period of oestrus.

DISCUSSION

Owing to the fortunate circumstance that this pig passed into the butcher's hands as a sexually mature animal just after an ovulation had occurred, we have had a unique opportunity to study the physiological state of the ovary; indeed, this is apparently the first sure case of glandular hermaphroditism in which there is direct evidence of the discharge into the deferent duct of germ cells from either gonad.

In the presence of a normal ovary containing very early corpora lutea, an ovum in passage through the Fallopian tube, and a full-sized uterus histologically normal, it seems more simple to consider this animal as functionally a female (at least as far as the internal genitalia are concerned) in which a local malformation had substituted a functionless testis and an epididymis for one ovary and the corresponding oviduct. In this respect the conditions are much like those of the previously described examples of true hermaphroditism in swine (now numbering about fifteen), in each of which the internal genitalia have been feminine as to gross morphology, with a more or less well-developed uterus and a testis or ovotestis in the anatomical position of the ovary. The opposite type of hermaphroditism—the presence of an ovary or ovotestis at the usual site of the testis, with the genital duct system resembling the male type—should it occur, is far less

likely to be observed by the anatomist because of the general custom of castration of boars intended for the butcher. In three of the four cases in man, however, which were summarized in the comprehensive review of L. Pick (1914), the hermaphrodite gland was found in the inguinal canal. The male gland of our specimen was not dissimilar to those of other cases. The close resemblance to the testes of ridglings, the absence of germ-cells, the relatively numerous interstitial cells, the remarkably complete epididymis, the persistent Wolffian duct, have all been commented upon in previous reports. So fully elaborated and indubitable a male apparatus as this must at once dispose of contentions such as that of Kermauner (1912), that the germ-lacking organs of supposed hermaphrodites are merely examples of non-differentiation from a neutral state of the gonadal primordium. In view of the current debate as to the early history of the germ-cells in mammals, great interest attaches to the question as to whether these gamete-free testes of hermaphrodites at any time in their development contained spermatogonia; and upon the answer to this depend the further questions as to why the ova seem always to survive at the expense of the spermatozoa, and in what manner the male germ-cells are inhibited; but these questions must await experimental attack or the chance discovery of embryonic stages of glandular hermaphroditism.

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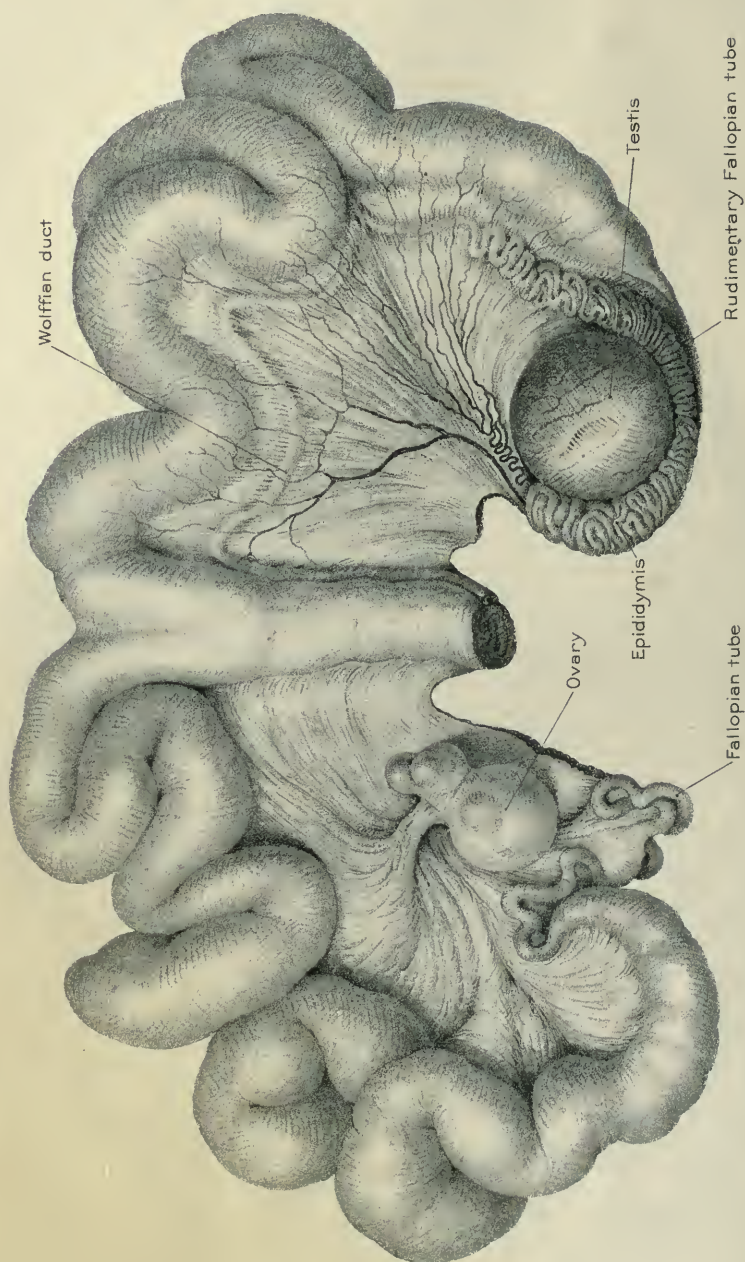
EXPLANATION OF PLATES

(1) General view of specimen; $\times 0.75$; (2) Section of testis showing relative proportions of tubular and interstitial cells; $\times 28$; hematoxylin and eosin. (3) Section of testis showing details of structure; $\times 1300$; iron hematoxylin. (4) Section of epididymis showing normal character of tissue; $\times 80$; hematoxylin and eosin. (5) Section of ovary showing several small Graafian follicles and proportions of tubular and interstitial cells; $\times 28$; hematoxylin and eosin. (3) Section of testis showing details of structure; $\times 1300$; iron hematoxylin. (4) Section of epididymis showing normal character of tissue; $\times 80$; hematoxylin and eosin. (5) Section of ovary showing several small Graafian follicles and part of an early corpus luteum; $\times 15$; hematoxylin and eosin. These figures were drawn directly on stone from the gross specimen and from the sections.

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TRUE LATERAL HERMAPHRODITISM IN A
 PIG WITH FUNCTIONAL OVARY
 G. W. CORNER

PLATE 1



General view of specimen; X 0.75. This figure was drawn directly on stone from the gross specimen

TRUE LATERAL HERMAPHRODITISM IN A
PIG WITH FUNCTIONAL OVARY
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PLATE 2

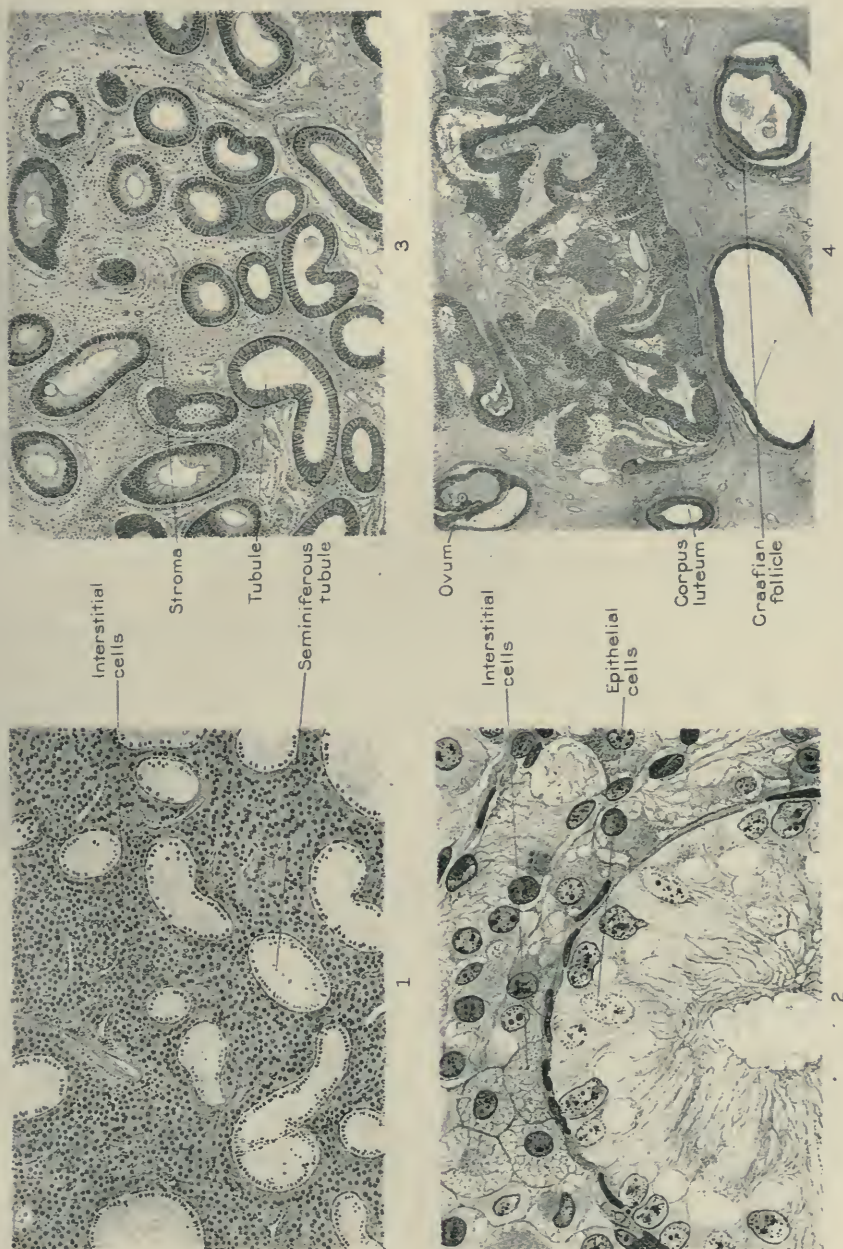


FIG. 1. Section of testis showing relative proportions of tubular and interstitial cells; X 28; hematoxylin and eosin. (2) Section of testis showing details of structure; X 1300; iron hematoxylin. (3) Section of epididymis showing normal character of tissue; X 80; hematoxylin and eosin. (4) Section of ovary showing several small Graafian follicles and part of an early corpus luteum; X 15; hematoxylin and eosin. These figures were drawn directly on stone from the sections.

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A CLINICAL AND PATHOLOGICAL STUDY OF CONTRACTED BLADDER¹

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The term contracted bladder is one which covers and includes a number of pathological conditions. It simply indicates a decreased bladder capacity, which may be due to lesions of various kinds. The distinction between the contracted bladder resulting from an acute inflammatory process and the type which is the site of a chronic inflammatory lesion is evident from a most superficial examination.

It is generally recognized that the majority of cases of bladder infection are secondary either to obstruction with or without residual urine or to some extravescical focus, such as the kidney, the seminal vesicles, the prostate or the sinus pocularis.

Every urologist is familiar with the rapidity with which a severe and resistant cystitis clears up following the removal of the primary focus. The bladder shows therefore a marvelous ability to eliminate infection once its source has been eradicated and this tendency is strikingly illustrated in many cases of tuberculosis. In most instances following the removal of the primary lesion, the inflammatory process in the bladder tends to heal provided it is not being reinfected from another focus. This peculiar ability of the bladder to take care of infection is so marked that some urologists have almost questioned the propriety of ever considering cystitis a clinic entity. This view is of course extreme, for after all outside foci of infection have been eliminated, there will remain a fairly large group of cases, in which the bladder infection does not disappear spontaneously but which

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responds to properly directed therapeutic measures. The cystoscopic picture in this group of cases shows a large range of variation, which includes a mere reddening of the mucosa, either localized or diffuse, areas of bullous edema, papillary formation and erosion or actual ulceration. Not infrequently in the same bladder, there may be a combination of all of these lesions. These cystoscopic findings usually signify only a mucous membrane lesion and give no index whatever regarding the degree or depth of the inflammatory process in the bladder wall. If the lesion is superficial and confined to the mucosa, it will usually disappear under local treatment. Those lesions which are resistant to irrigations or instillations will frequently be benefited by the application of strong solutions of silver nitrate. Where, however, this is difficult or impossible, the institution of daily hydraulic distension has in our experience yielded most gratifying results. In refractory cases where the lesion involves only the mucosa, systematic hydraulic distension with an attempt to increase the bladder capacity from day to day will gradually lead to resolution of the inflammatory process and a return of the bladder mucosa to normal. When, however, following the hydraulic distention, recontraction of the bladder occurs, one may be reasonably certain that he has been dealing with more than a mucous membrane lesion and that the pathological process involves the deeper layers of the bladder wall.

In these cases of cystitis, where the mucous membrane is involved, there is present in the urine varying amounts of blood, pus and bacteria. This is in striking contrast to the urinary findings in cases where the lesion is largely submucous. In this latter group the symptoms may be most distressing and severe and the pathological change in the urine slight or absent.

In 1913, Hunner reported a group of cases of marked contracture of the bladder. The symptoms presented by these patients were out of all proportion to the comparatively slight or negative changes in the urine and the cystoscopic findings often very indefinite. He made this report under the title "Elusive Ulcer of the Bladder." They really represent a group of cases in which the mucous membrane lesion has

disappeared, the predominant pathological factor being the inflammatory process in the deeper layers of the bladder wall.

Nitze had previously described apparently the cystoscopic picture in this form of cystitis and since Hunner's report, Geraghty, Keene and more recently Kretschmer and Bumpus have called attention to this pathological condition.

It should be noted in this connection that Nitze's description of the condition consists simply of a cystoscopic observation. To Hunner belongs the credit, not only for making a careful study of the condition but for having first proposed and successfully carried out in a considerable series of cases a rational surgical procedure.

The value of Hunner's work, which was carried out independently of the observation of Nitze, is emphasized upon reflection, that up to the time of his report, the pathological significance of this not uncommon lesion was unappreciated and all efforts directed toward a relief of the condition unavailing.

During the past five years, twenty-six cases presenting this lesion have been treated in the Brady Urological Clinic. In this series only three have occurred in females. The small proportion of women is probably explained by the fact that the great majority of cases treated in the clinic are male. The cases reported by Hunner and Kretschmer all occurred in females but Bumpus has recently reported five cases occurring in the male. It seems probable that the condition occurs with about equal frequency in both sexes.

Of the twenty-six patients with this type of contracted bladder, the ages were as follows.

Ten to twenty years.....	1
Twenty to thirty	4
Thirty to forty.....	6
Forty to fifty.....	7
Fifty to sixty.....	8

SYMPTOMATOLOGY

It is at once evident from a study of the cases comprising this series that the most prominent symptoms are urinary

frequency and pain. These symptoms were present in every case and their duration ranged from four months to nineteen years. The frequency in eleven of the cases was extreme, amounting almost to incontinence, the patients having an almost constant desire to void. This symptom was present both day and night, although in the majority of cases it was somewhat more aggravated when the patient was up and about.

In four of the cases there was definite obstruction to urination, all of them having contractures of the vesical orifice. In two others the urinary stream was frequently interrupted, probably due to spasm of the vesical sphincter.

Severe suprapubic pain, when the bladder is allowed to distend, has been a symptom common to all of the cases. In some cases, this has been referred to the right or left of the midline, subsequent examinations showing the lesion in the corresponding half of the bladder. The pain on distension has usually been described as severe or cutting.

Many of the cases have noted an intensification of the suprapubic pain at the beginning of urination, while others have experienced a burning sensation in the neck of the bladder, perineum and glans penis at the end of the act which sometimes persisted for several minutes. In one case, this was associated with marked urgency and an intense desire to void more urine. In only one case was the pain during urination referred to the rectum.

A history of hematuria coming on independently of instrumentation was elicited in seven cases. In one of these it was quite profuse and followed exertion. Another case gave a history of passing a small clot two weeks before admission. Two others volunteered the information that they had noticed slight hematuria occasionally while in the remaining four cases the hematuria was terminal and usually associated with marked straining at the end of urination.

In ten of the cases, the urine was negative for pus and microorganisms, while the urine in four of the cases showed on centrifuging a few leucocytes and red blood cells. The remaining sixteen cases showed varying amounts of pus and micro-

organisms, the infection in fifteen being a bacillus, while in one case a staphylococcus was found. In only one of the cases was the presence of renal infection demonstrated, this case having unilateral pyelitis, which cleared up on pelvic lavage. In two of the infected cases in the series, ureteral catheterization was not carried out.

The history of gonorrhea was obtained in eight of the cases, but in only two did this infection bear any time relationship to the development of the bladder symptoms. In one of these cases the gonorrhea was complicated by acute epididymitis. At the end of three months urinary frequency, urgency and terminal hematuria began. These symptoms persisted despite treatment, gradually becoming more pronounced and at the time of his admission three years later, his bladder symptoms were extreme.

Another patient whose gonorrheal infection was apparently complicated by an acute posterior urethritis and trigonitis had been operated upon eleven years later for urethral stricture, an external urethrotomy being done. His bladder symptoms had begun two years after his gonorrheal infection and had gradually progressed, being unrelieved by the cure of the urethral stricture.

CYSTOSCOPIC FINDINGS

A constant and prominent feature of all the cases is a diminution of the bladder capacity, together with the production of severe suprapubic pain when an attempt is made to introduce fluid beyond this amount. At the original examination of these twenty-six cases the bladder capacity was as follows:

50 cc. or under.....	9
50 cc. to 100 cc.....	7
100 cc. to 200 cc.....	7
200 cc. to 300 cc.....	3

The cystoscopic appearance of the lesion varied considerably. In twenty of the cases the change in the mucosa was very slight, the patient's symptoms being out of all proportion to the apparent insignificance of the lesion. The lesions were frequently so indefinite that but for the fact that the condition was sus-

pected, it might easily have been overlooked. A slight or intense reddening of the mucosa, ranging from a few millimeters to several inches in diameter was frequently the only abnormality noted. In other cases close inspection of the lesion showed a definite puckering, indicative of a fibrous change in the sub-mucosa. The center of this type of lesion is often paler than the periphery which may be intensely red. Not infrequently during the cystoscopy the lesion which at first was quite indefinite becomes very much more evident. It is now intensely red and often appears slightly elevated above the surrounding mucosa. When the bladder, which is the seat of such a lesion, is subjected to marked distension, bleeding at the site of the lesion invariably occurs. The mucosa which, up to this time, has been intact, now shows bleeding fissures which at subsequent cystoscopies are seen to be covered with muco-pus. In certain cases, particularly those having an infected urine, a definite ulcer may develop at this point.

In four of the cases, definite ulceration was noted, the ulcer being irregular, superficial, covered with muco-pus and surrounded by a zone of hyperemia and edema.

In thirteen of the cases the lesion was single, in seven two lesions were found, and in three, three or more inflammatory areas were noted. The location of the lesion was anterior wall ten cases, antero-lateral walls two, lateral walls six, and posterior wall five.

In three of the cases the bladder contraction was extreme, the capacity being less than 30 cc. When an attempt was made to introduce more fluid, bleeding occurred. From the view obtained, the mucosa was everywhere thickened and intensely inflamed but no definite ulcerations were noted.

In another case, in addition to the above findings, a small ulcer was found on the anterior wall.

DIAGNOSIS

While the symptomatology of no bladder disease can be considered pathognomonic, the symptoms presented by patients suffering from this type of contracted bladder are certainly very

valuable leads to diagnosis. The history of long-standing frequency and suprapubic pain on bladder distension, in the absence of any symptoms of obstruction, is strongly suggestive of the condition, particularly in those cases having an uninfected urine. The marked contraction of the bladder, the reproduction of the pain complained of by the patient and the cystoscopic findings complete the diagnosis. In these cases in which no actual ulceration is present and in which the lesion is quite indefinite, over-distension of the bladder will frequently cause bleeding at the site of the lesion and aid in its localization. We have noted not infrequently that many lesions which were very indefinite cystoscopically became most striking when the bladder was opened at operation. The area of involvement not infrequently presents deep bleeding, often irregular fissures, which extend into the sub-mucosa. In some cases in which the bladder has been greatly distended, the mucosa and submucosa may be missing throughout quite large areas.

The marked difference between the cystoscopic appearance of the lesion and that at operation is very probably due to over-distension, sponging, etc. It is impossible therefore from the the cystoscopic appearance to form any accurate idea of the extent of the lesion, which is so intensified when the bladder is opened.

PATHOLOGY

In fourteen cases operated upon, the bladder showed more or less thickening of its wall. In some of these cases, it was extremely thick at the site of the lesion, the inflammatory process having extended through the coats of the bladder and not infrequently involving the perivesical tissues. In eight of the cases, the bladder wall was quite thin, being only very slightly thicker at the point of inflammatory involvement. The lesion in these cases was therefore confined to the sub-mucosa.

Study of the epithelial changes are quite unsatisfactory, as one rarely obtains a specimen in which the epithelium is intact and it is unsafe to draw conclusions regarding the partial loss of epithelium unless one is able to remove the specimen

without in any way traumatizing the surface of the tissue removed. The epithelium of the bladder mucosa is rubbed off with very slightest trauma. Before one can depend upon the microscopical changes in the epithelium, it would be necessary to harden the specimen in situ. We have not been able to obtain a specimen in which we could speak with any certainty that the loss of epithelium bore any relation to the lesion.

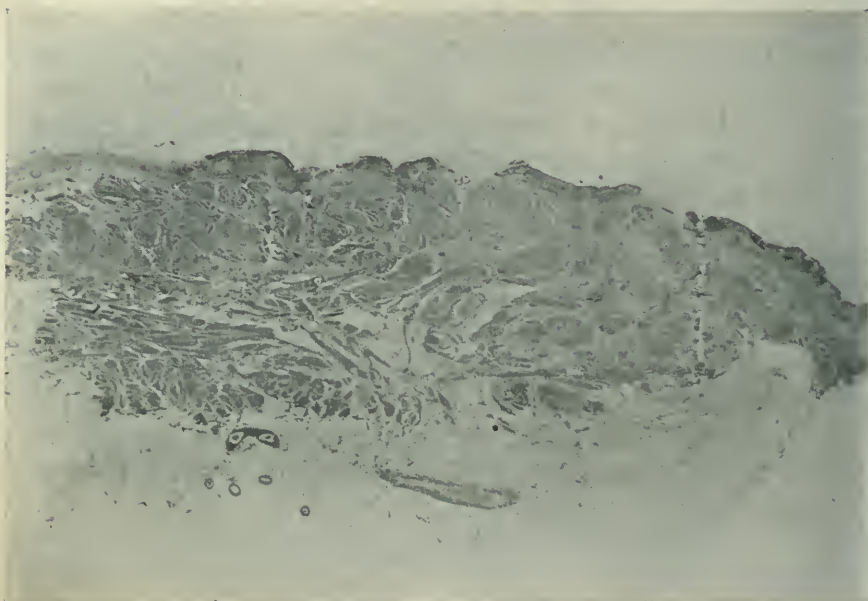


FIG. 1. PHOTOMICROGRAPH OF OPERATIVE SPECIMEN SHOWING A THICKENED SUBMUCOUS FIBROUS LAYER WHICH IN PLACES HAS BEEN TORN AS A RESULT OF OVERDISTENSION OF THE BLADDER

The striking and important lesion in all of the cases in which the tissue has been studied has been a fibrosis of the sub-mucosa, the thickness of the layers varying considerably. The mucous membrane in these cases rests directly upon the dense scirrhous layer instead of, as in the normal bladder, upon the loose areolar tissue.

When the bladder is over-distended in these cases, the mucous membrane cracks as this fibrous layer is inelastic. In most cases

beneath this fibrous lamella there is round celled infiltration of varying degrees of intensity, in no way dissimilar from ordinary cases of chronic cystitis. Sometimes the inflammatory process can be followed down in between the muscle layers and even as far, in exceptional cases, as the serous coat. Where this deep invasion occurs one usually finds the lesion thick-walled. In those cases in which a chronic inflammatory process is limited to sub-mucosa, it is usually found that the bladder wall is rarely if any thicker than normal. In most cases a marked congestion and dilatation of the blood vessels and extravasation of blood in the tissues are observed. How much of this is due to trauma is difficult to decide.

The associated and constant lesion in the disease is apparently the sub-mucous fibrosis, sometimes thick, sometimes thin, rarely if ever replacing the areolar tissue entirely. This layer is extremely dense in most cases. The microscopic picture as a whole differs scarcely at all from the average changes seen in simple chronic cystitis, except in the formation of the fibrous submucous layer.

TREATMENT

Experience has shown that nothing short of operation has accomplished any permanent results in those cases in which more than the bladder mucosa was involved. In cases therefore in which the findings are such as to indicate an involvement of the submucous or deeper layers, it is futile to temporize with conservative treatment. If the lesion lies in portions of the bladder which can be resected, this operative procedure is to be recommended. If, however, the areas of involvement cannot be removed, deep cauterization should be practised.

If the findings on cystoscopy make it difficult to differentiate between a superficial lesion and one involving the deep layers of the bladder, a conservative course of treatment, such as vesical distensions, instillations and irrigations may be employed. This plan of treatment in our hands, however, has proved most unsuccessful, so far as permanent cure is concerned.

In certain cases in which the entire bladder is involved in this process, which are complicated by superficial ulceration, removal

of the ulcer will not infrequently relieve the patient's pain, although only slight improvement, so far as urinary frequency is concerned, can be expected.

As we have previously stated, these lesions resolve themselves into two types, one in which the bladder is thin, the pathological lesion involving principally the submucosa. In some of these

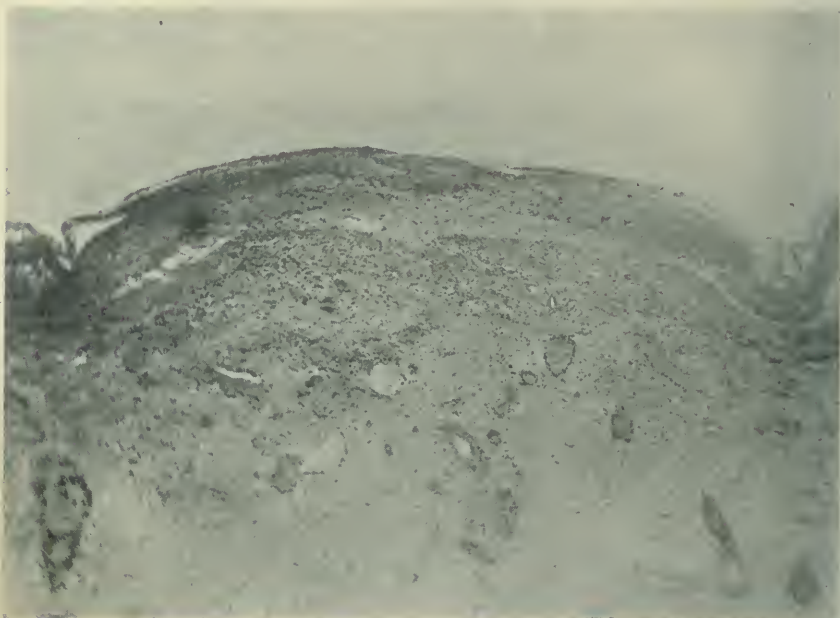


FIG. 2. PHOTOMICROGRAPH SHOWING A THIN AND INTACT LAYER OF FIBROSIS LYING UPON A SOMEWHAT THICKENED SUBMUCOSA.

The bladder in this case was not subjected to overdistension preliminary to operation.

cases, the lesion occupies so large a portion of the bladder that resection is either too hazardous or impossible. In these cases deep cauterization with destruction of the mucosa and sub-mucosa has resulted in marvelous improvement and cure. It has further been our experience that where the bladder is thick-walled and where the lesion involves all the layers of the bladder wall, the area of involvement is usually localized and

usually lends itself admirably to resection. Further experience may show that deep cauterization alone may be sufficient to effect relief of the condition present. We have not felt justified, however, in cauterizing where resection has been possible.

The type of treatment carried out in this series of 26 cases may be summarized as follows: Twenty-two of the cases were operated upon and in four the treatment consisted solely of vesical distensions, instillations, fulguration and the application of silver nitrate to the area involved. Fifteen of the operated cases were treated by resection while in four, because of the extent of involvement and the fact that the lesion was apparently superficial, deep cauterization was employed. In one of the earlier cases an extensive although superficial area was treated with the silver nitrate stick. In three cases in which the process involved practically the entire bladder, an associated contracture of the vesical orifice was found. This was relieved by a punch operation and the bladder mucosa which was thickened and inflamed was thoroughly curetted. It is interesting to note that of the eleven cases treated conservatively, seven were subsequently operated upon.

RESULTS

The results in the fifteen cases in which radical excision of the inflammatory area was carried out show in thirteen complete relief so far as pain is concerned. In seven there is normal frequency of urination while in the remaining six, in all of which there was a diffuse cystitis, more or less urinary frequency persists. Two of the fifteen patients died following operation, one of bilateral pyelonephritis, the other of paralytic ileus.

In five of the cases treated by cauterization, the results in four are encouraging for this type of treatment in selected cases. The one failure was a case proved subsequently to have a lesion involving all of the layers of the bladder wall. Cauterization in this case was followed by no improvement and resection has recently been carried out.

In two women of the series, one of whom was treated by resection, the other by cauterization and resection, operation was

followed by more or less obstruction to urination as evidenced by the development of residual urine of from 100 to 200 cc. In one of these cases the condition was thought to be due to contracture of the vesical orifice and improvement followed a partial division of the sphincter. In the other case the cause of the retention was not determined.

The four cases in which the treatment consisted solely of hydraulic distension and local applications, there has been marked improvement in urinary frequency and pain. In none of these, however, has the improvement been permanent and it seems probable that a complete cure will not be realized until more radical measures are instituted.

The following cases are cited as illustrative not only of the symptomatology and pathological findings of this condition but the response to various methods of treatment.

Case 1. No. 9272. Male, age twenty-seven. This patient was first seen December 9, 1920, his complaint being frequency and painful urination. This patient's urinary symptoms dated back to May, 1915, at which time he began to have some urinary frequency and pain which was referred to the neck of the bladder. The pain was usually more marked as the bladder was emptying and would sometimes last for three quarters of an hour after urination. He gave a history of only one attack of hematuria. During the year prior to his admission, his frequency became somewhat more marked, it being necessary for him to void at hourly intervals. He suffered also from some suprapubic pain on vesical distension, as well as pain in the neck of the bladder during urination.

On cystoscopic examination the bladder capacity was 100 cc. On the anterior bladder wall, just behind the prostatic orifice, were two very definite ulcerations measuring about 3 cm. in diameter. The region of the ulceration was slightly elevated and the mucosa in the immediate vicinity intensely red. Study of the bladder urine showed no infection.

During the following six weeks the patient received daily vesical dilatations, and his bladder capacity increased to 375 cc. and there was marked symptomatic improvement.

Cystoscopy on February 11, 1921, showed some improvement in the appearance of the lesion on the anterior bladder wall, although there was still slight ulceration and reddening.

Patient was last heard from April 1, 1921. He had been quite comfortable until one week before when he had a gradual return of urinary frequency and pain.

Case 2. No. 5289. Male, aged twenty-three, admitted July 1916. This patient gave a history of two attacks of gonorrhea, one in 1911 and the second in 1915. He stated as long as he could remember, he had had some urinary frequency but that during the year prior to his admission his bladder had become very much more irritable. He was, however, able to hold his urine for an hour during the day and one and a half hours during the night, although when asleep he frequently had slight incontinence. When the bladder became distended, he suffered from some suprapubic pain.

Cystoscopy: Two small red areas were seen in the region of the air bubble. The remainder of the bladder appeared to be quite normal. Study of the patient's urine showed some pus and bacilli. Attempt at ureteral catheterization was not successful.

This patient received daily treatments consisting of hydraulic distensions of the bladder and at the end of two weeks his capacity was 110 cc. He was seen two years later, at which time there was some improvement in his former symptoms.

Cystoscopy at this time revealed lesions on the anterior wall which were practically identical to those seen on the first admission. His bladder capacity was 80 cc. The patient received bladder dilatations for the following two weeks and his bladder capacity was increased to 130 cc. He was advised to continue his dilatations daily.

This patient was heard from in April 1921. He reports his condition as improved but states he is able to hold his urine for only two hours during the day and night. He is now complaining of pain in the suprapubic region, when the bladder is allowed to distend and at the end of urination.

Comment: The employment of daily hydraulic distension with local treatment consisting of direct application of strong silver nitrate or the high frequency spark to the site of the lesion has, in many instances, resulted in marked symptomatic improvement with an increase in bladder capacity approaching normal. In all cases, however, in which subsequently the lesion had been proved to involve layers other than the mucosa, there has been a recurrence of symptoms and the patient has presented a clinical

picture similar to or worse than originally noted. This type of treatment is applicable therefore only to those cases in which the mucosa is alone involved.

Case 3. No. 9600. Male, aged sixty-five, admitted April 13, 1921, with the history of having an attack of urinary frequency associated with pain in the suprapubic region and the deep perineum a year previously. These symptoms persisted and during the six months prior to his admission, he was voiding every few minutes, the bladder, if allowed to distend, causing him extreme suprapubic pain.

On examination, the bladder was found to have a capacity of less than 60 cc., the patient complaining bitterly when more fluid was introduced. Under ether anesthesia a considerably greater capacity was obtained and a fairly satisfactory cystoscopy carried out. On the posterior bladder wall was a large area of papillary cystitis. The lateral walls while edematous were not particularly red; the bladder urine was rather badly infected.

At operation on April 15 the bladder was subjected to rather marked overdistension, and upon opening it the mucosa of the posterior bladder wall over a large area was irregularly torn and bleeding, a picture more or less typical of these lesions when the bladder is overdistended. Because of the extent of the lesion together with the fact that the bladder did not appear to be very thick-walled, suggesting a rather superficial lesion, a resection was not attempted, the lesion being vigorously burned with the electro-cautery. Investigation of the vesical orifice showed a rather marked contracture which was relieved by a "punch."

The suprapubic wound has now been healed three weeks and the patient is voiding at normal intervals without pain.

Case 4. No. 7114. Female, aged forty-two, first examined on August 5, 1918. Her urinary symptoms dated back fifteen years at which time, two weeks after childbirth, she experienced great difficulty in voiding. She noticed no further trouble until the last year, during which time she had suffered intense pain and spasm in the suprapubic region, particularly when the bladder became distended. There had also been very marked frequency of urination, it being necessary for her to pass her urine every few minutes. She gave no history of hematuria except on one occasion following a bladder irrigation. Since the onset of her recent symptoms, there has been no hesitancy or other obstructive symptoms.

Her general physical examination was quite negative. The bladder urine was grossly clear but on microscopic examination a few pus cells and *B. coli* were found. On cystoscopy, the bladder capacity was less than 50 cc. On the posterior bladder wall there was an intensely red area, slightly elevated, more or less circumscribed, and scattered here and there with tiny, superficial ulcerations.

At operation on August 9, 1918, it was found that under ether the bladder capacity was 300 cc. On examination there was found on the anterior wall, to the left of the vesical orifice, a localized, intensely red area. Another smaller area was found on the posterior wall, between the two ureters. This latter area involved a portion of the trigone and extended posteriorly for some distance. No definite ulceration was made out at operation. The remainder of the bladder was normal. Because of the position of the inflammatory area on the floor of the bladder, which involved a portion of the trigone, it was considered inadvisable to excise this area. The area to the left of the vesical orifice was resected and the large area on the posterior bladder wall was thoroughly cauterized.

The portion of bladder wall resected was little if any thicker than normal. Microscopic examination of the section shows an absence of the bladder epithelium. Throughout its entire extent is seen a very thin, apparently dense area of fibrosis replacing the more superficial layers of the submucosa. This in places is torn and ragged, apparently the result of overdistension. The remainder of the submucosa which appears to be somewhat thickened shows many dilated vessels and in areas rather dense infiltrations of small round cells.

The post-operative course was quite uneventful and at the time of her discharge on October 2, 1918, the patient was symptomatically very much improved. She was free from the pain she had suffered before operation and her bladder capacity was 90 cc. Her bladder urine was quite cloudy and it was thought at the time that her diminished bladder capacity may have been caused by the cystitis resulting from the suprapubic operation.

The patient was again seen on May 15, 1919. Her bladder was no longer painful but the suprapubic incision which had broken open on several occasions was now draining a small amount of urine. The patient voided 130 cc. of urine.

Cystoscopy at this time showed the bladder in the region of the trigone to be quite irregular with a septum formation to the left of the mid-line in the region where the resection was done. The bladder mucosa

was quite pale, there being none of the red areas seen originally. The condition was thought to be one of contracture of the vesical orifice in view of the fact that about 100 cc. of residual urine were found. Her treatment at this time consisted of high dilatations of the vesical orifice and at the time of her discharge, November, 1919, the suprapubic wound was healed. The patient was able to void at the time of her discharge 90 cc. but on being catheterized immediately after 130 cc. of urine were obtained, the bladder capacity therefore being 220 cc.

The patient again returned to the hospital March 19, 1920, the suprapubic fistula having reopened a short time after leaving the hospital. Her residual urine at this time was in the neighborhood of 200 cc. She suffered from practically no pain in the region of the bladder. The vesical orifice was divided with the punch instrument and at the time of her discharge, the suprapubic wound had been healed for four days, and the patient was emptying her bladder completely. She was able to hold her urine two and one-half hours without pain.

Comment: This case was treated by a combination of cautery and resection. A study of the specimen removed, however, suggests that a favorable result would have followed the employment of the cautery alone. Operation in this case was followed by symptoms of urinary obstruction and the development of residual urine, a post-operative complication noted in another woman in the series having an extensive resection. The condition in this case was thought to be due to contracture of the vesical orifice, as marked improvement followed high dilatations and partial division of the sphincter. The cause of the obstruction in the other case was not determined.

Case 5. No. 5751. Male, aged forty, was first seen in February, 1917. He gave a history of an attack of gonorrhea in 1905 which was complicated apparently by acute posterior urethritis. Two years later he developed symptoms of urinary obstruction and was operated for urethral stricture ten months before admission. In February, 1915, he began to suffer from urinary frequency and dysuria, together with marked suprapubic pain on vesical distension. There is no history of hematuria.

On cystoscopy, there was no residual urine and the bladder capacity was 100 cc. On the left lateral wall of the bladder, midway between the apex and the vesical orifice, the mucosa over an area measuring 2.5 by 3.5 cm. was elevated and the seat of a hemorrhagic and papillary

cystitis, in the center of which was a small area of ulceration with adherent muco-purulent material. On distension of the bladder to 100 cc., this region bled quite freely. This lesion was considered suspicious of tuberculosis and this view was apparently strengthened by the presence of considerable pus in the bladder urine without demonstrable pyogenic organisms. Repeated studies of the bladder urine, however, were negative for the tubercle bacillus and ureteral catheterization ruled out the possibility of renal tuberculosis.

At operation on March 14, 1917, after the peritoneum had been pushed back so as to expose extravasically the left lateral wall, the operator could feel distinctly the area involved in the inflammation. The perivesical tissues were adherent at this point and in addition a distinct induration could be detected in the bladder wall. Upon opening the bladder, the area noted at cystoscopy showed an irregular margin and a surface intensely red and bleeding. It was quite readily excised, the specimen measuring 6 cm. in diameter. The remainder of the bladder was normal. The defect was then repaired by a continuous catgut suture and the bladder drained by a rubber tube inserted at the apex.

Pathology: The specimen removed at operation shows a diameter of two to three times that of the normal bladder wall. The surface is intensely red and fissured. Microscopically, an absence of the bladder epithelium is noted and that portion normally lying immediately beneath is very ragged and irregular. At several points is seen a dense wavy line of fibrous tissue which at intervals is missing, being torn off apparently as a result of overdistension of the bladder. The submucosa proper is very vascular and the vessels apparently quite dilated. Throughout the submucosa and in places extending well down into the muscular layers are many small round cells, the infiltration at certain points being quite dense.

Result. The recovery in this case was uneventful. When heard from April 22, 1921, he was free of bladder symptoms.

Case 6. No. 8516. Male, aged fifty-two, seen February 14, 1920, giving a history of urinary frequency for fifteen years. During the fifteen months prior to his admission, his symptoms had become more pronounced and it was necessary for him to void at hourly intervals. When the bladder was allowed to distend, severe suprapubic pain resulted. With these symptoms there had been increasing difficulty in voiding and three days before admission he developed acute retention and had to be catheterized.

On cystoscopy, there was no residual urine and the bladder capacity on forced distension was 150 cc. The bladder urine was perfectly clear and uninfected. In the posterior wall to the right of the midline was found an irregular, more or less linear red area, and behind each ureteral orifice, similar although smaller areas were seen. The remainder of the bladder mucosa was normal in appearance. There was no trabeculation and no trigonal hypertrophy. In view of the history of urinary obstruction and recent retention, notwithstanding the absence of residual urine and trabeculation, the condition was thought to be a contracture of the vesical orifice and a punch operation was carried out. During the following six weeks the bladder was dilated by daily hydraulic distension, the capacity reaching 360 cc.

Cystoscopy April 5, 1920, revealed very little change in the appearance of the inflammatory area, except that possibly the surface lesion was somewhat more pronounced.

During the next eight months there was no difficulty in voiding. The interval between voidings was from two to three hours and the patient experienced practically no pain except at times when the bladder became greatly distended. About January 1, 1921, his bladder symptoms suddenly became much aggravated. There was increasing difficulty in starting the urinary stream and a marked increase in frequency and suprapubic pain.

On cystoscopy January 21, 1921, the bladder capacity was 60 cc. Three superficially ulcerated areas were found in the same positions noted in former cystoscopies.

On January 26, 1921, after overdistension with air, the bladder was opened revealing three bleeding areas back of the trigone. One of these lying quite far posteriorly presented an irregular linear fissure 5 cm. in length which apparently extended into the submucosa. Similar, although somewhat smaller lesions, were seen back of the ureteral orifices. Because of the extensive involvement, resection was not attempted and the areas were thoroughly cauterized. At the end of three weeks the patient was discharged, cystoscopy at this time showing the cauterized areas to be healed and apparently normal except for some edema.

Two weeks later there was a return of frequency and pain, and when seen March 24, 1921, he was voiding every two to three minutes. The urine was clear and not infected. Cystoscopy revealed an irregular, edematous, superficially ulcerated area about 3 cm. in diameter, a short distance back of and to the right of the right ureteral orifice. The

area involved a portion of the bladder formerly the site of one of the smaller lesions previously noted. The posterior bladder wall as well as the region of the left ureteral orifice were normal in appearance.

At operation April 27, 1921, the bladder was first carefully freed from the right side as far as possible posteriorly. It was then opened and a wide, elongated, irregular ulcer, measuring 4 cm. in length by 0.5 cm. in width, was found extending from a point about 1.5 cm. back of the right ureteral orifice on to the right lateral wall. Another ulceration 1 cm. in length was found to the right of this. The bladder wall in this region was greatly thickened, indurated and very adherent to the perivesical tissues. The remainder of the bladder was normal in appearance and the other areas formerly treated with the cautery gave no indication of inflammatory change and the bladder wall at these points seemed to be of normal diameter and consistence. The area of ulceration was excised with a wide margin.

Pathology: The operative specimen which measured 8 by 4 cm. was quite firm and at least three times the normal thickness of the bladder wall. The mucous surface presented several deep, elongated blood stained fissures which extended apparently well into the submucosa. Microscopically, the mucosa was lacking, the superficial surface of the section showing the thin fibrous lamella, torn in many places from the overdextension of the bladder at operation. The submucosa which appeared to be three to four times its normal diameter was diffusely infiltrated with small round cells. This layer showed an increased vascularity with considerable extravasation of blood. The muscle layer showed only here and there a moderate round celled infiltration, but the separate muscle bundles were frequently widely separated, suggesting an edema which probably explained the great increase in the diameter of the specimen.

Result: At cystoscopy on June 18, 1921, the bladder capacity was 80 cc. The posterior and lateral walls were perfectly normal in appearance. On the anterior wall at the point where the bladder was drained was an area of reddening, a not uncommon finding in recently healed suprapubic cases. The patient was voiding at hourly intervals with no suprapubic pain on vesical distension.

Comment: This patient presented in addition to the usual symptoms of this type of contracted bladder others occasionally met with, namely, hesitancy, slow stream and finally complete retention. The obstructive symptoms were at first thought to

have been caused by a contracture of the vesical orifice but a study of the specimens removed with the punch instrument shows only a moderate prostatitis. The obstructive symptoms in this case are thought to have been due to a sphincteric spasm reflexly produced by the very irritable and painful bladder. The case illustrates further the futility of the dilatation treatment as well as the favorable response of two of the lesions to deep cauterization. Whether or not the area finally resected represents a recurrence or the further development of a lesion incompletely destroyed by the cautery is uncertain. The prompt recurrence of symptoms, together with the ultimate pathological findings, rather strengthen the latter possibility.

SUMMARY

The essential lesion in the condition variously described as "elusive ulcer," "localized cystitis," "interstitial cystitis," "pan-mural cystitis," etc., is a sub-mucous fibrosis. In most cases other evidences of inflammatory change are noted in the different layers of the bladder wall, but these differ in no respect from in the average case of chronic diffuse cystitis.

The cardinal symptoms of the condition are urinary frequency and pain, referred chiefly to the suprapubic region and resulting from overdistension of the bladder.

The diagnosis is based upon the history, the finding of a diminished bladder capacity, with urine not infrequently sterile, the production of intense suprapubic pain when an attempt is to introduce fluid beyond its capacity and cystoscopic findings often comparatively slight and out of all proportion to the clinical picture presented. In cases having sterile urine, cystoscopy may reveal insignificant and trivial areas of reddening of the mucosa at one or more points; in other cases slight puckering is noted, while in cases having an infected urine, superficial ulceration may be present. The occurrence of bleeding at the site of the lesion, following overdistension, is strongly suggestive of the condition, but the production of linear or irregular tears in the mucosa by this procedure is almost pathognomonic of it. The bladder capac-

ity when the patient is deeply anesthetized, approaches normal, a point of differentiation between the cases in which the lesion is more or less localized and those cases in which practically the entire bladder is involved. In the latter group the bladder is inelastic and the capacity under anesthesia shows very little increase over that when the patient is awake.

Hydraulic distension of the bladder, local application of various drugs, high frequency, etc., have in our experience been unproductive of permanent results in this group of cases.

When the lesion occupies a portion of the bladder permitting resection, this procedure should be employed. In those cases in which resection is not feasible, deep cauterization should be practised.

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PLATE 1

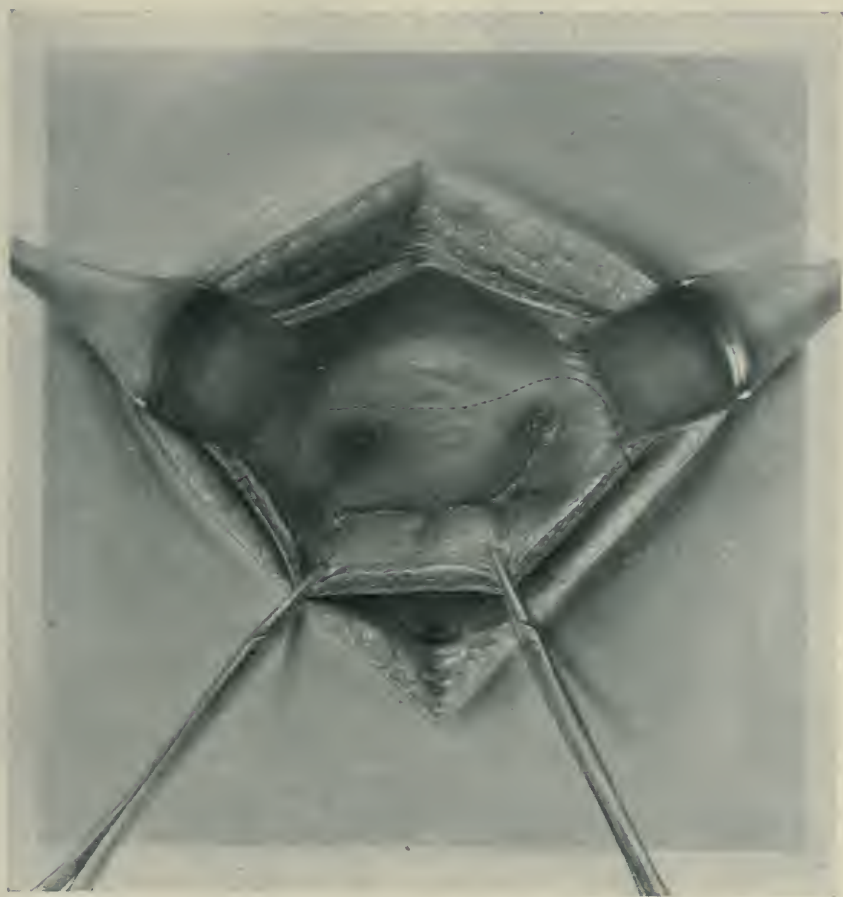
OPERATIVE SPECIMEN SHOWING SUBMUCOUS HEMORRHAGE AND DEEP FISSURES
RESULTING FROM OVERDISTENSION OF THE BLADDER



PLATE 2

OPERATIVE VIEW OF LESION SHOWN IN PLATE 1

The dotted line indicates the anterior margin of specimen excised



COMBINED TUMORS OF THE KIDNEY

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Combined renal tumors are rare. Their occurrence, however, has been reported in a few instances. What is probably the first discussion of the subject has been recently presented by Berry. In his interesting paper, he described four cases in each of which two tumors were found within one kidney.

In case 1, a woman of forty-three years, there was found a large mass arising from the right kidney. On section, the gross appearance of the tumor was suggestive of two types of growth. Histological study revealed the presence of adrenal cell carcinoma and fibrosarcoma, in some areas separate and in others intermingled.

In case 2, a woman of thirty-five, a left nephrectomy was performed for the removal of a tumor. There was no gross evidence of combined growth. The microscopic findings, however, were those of papillary adenocarcinoma, and fibrosarcoma. There was no apparent blending of the two.

In case 3, a man of seventy-two, a large right kidney was removed at operation. The tumor which was found was demonstrated histologically to consist of two types of neoplasm, hypernephroma and leiomyosarcoma. The two tumors grew separately.

Case 4, a man aged fifty-one, is mentioned but the record is not described in detail. An adrenal tumor and a renal cell adenoma were found in a kidney at autopsy.

In the first three of these cases, epithelial and sarcomatous types of neoplasm were associated. With one exception microscopic study was necessary to determine definitely the presence of the combined tumors. The possibility of the sarcomata arising as the result of some influence exerted upon their stroma by the epithelial growths, was mentioned, but discredited by the author. He was firmly of the opinion that two distinct and unrelated tumors existed in each case.

We have found no other records of true multiple tumors of the kidney. To be sure, as noted by Berry, in 1891 Beneke described two cases of hypernephroma certain malignant areas of which presented sarcomatous characteristics. He believed in the possibility of the development of sarcoma from adrenal tissue. With so much lack of agreement in the matter of nomenclature and with the whole subject of adrenal cell tumors of the kidney so much in dispute, these can hardly be accepted with certainty as instances of combined growth.

It is our purpose to present two cases of true combined renal tumors. Of the separate character of the associated neoplasms, there can be no doubt.

*Case I.*¹ A Nova Scotian hotel-clerk, aged fifty-two years, entered the Peter Bent Brigham Hospital on September 25, 1920, complaining of hematuria and backache.

The family history was unimportant. The patient's wife had died of gastric carcinoma. There had been no children. There was a past record of excellent general health. The patient had had measles in childhood, and influenza in more recent years.

In August, 1919, one year before admission to the hospital, the patient observed that his urine was red in color. After that time, hematuria recurred intermittently and on frequent occasions. For the month before hospital entry all of the voided urine contained blood. No clots were passed. Hematuria was never accompanied by increased frequency of urination, nor by dysuria. Occasionally, however, the bleeding was preceded for a day or two by dull, aching pain in the left lumbar region. During the period of his difficulties the patient lost approximately twenty-five pounds in weight, and he complained also of increasing weakness.

Examination found a well developed, obese male of middle years, who gave no evidence of distress or pain, but whose appearance was suggestive of long-standing illness. The skin was rather loose and flabby as though there had been recent loss of weight. The face was pale, and the mucous membranes were of poor color. The temperature, pulse, and respirations were normal. The routine physical examination

¹ These two cases were briefly presented by Dr. W. C. Quinby, at the November meeting of the New England Branch of the American Urological Association, the transactions of which are published in the *Journal of Urology*, 1921, v, 133-169.

was essentially negative, although the degree of obesity rendered abdominal palpation rather unsatisfactory.

The urine was smoky; acid; specific gravity, 1.022. There was a large trace of albumin; no sugar. Microscopy: Many white blood cells; a few red blood cells; an occasional hyalin cast. Excretion of phenol-sulphonephthalein: 60 per cent in two hours. Hemoglobin: 90 per cent; white blood count: 8000. Blood pressure: 140/85.



FIG. 1. FROM CASE I

Low power photomicrograph showing papillary carcinoma of the renal pelvis

Cystoscopic examination found no significant bladder abnormalities. Both ureters were readily catheterized. Clear urine was obtained from the right side; a very slight, blood-stained flow was obtained from the left. Microscopic examination of the urine of the right kidney was negative. A study of the output of the left kidney revealed clumps of epithelial cells, and occasional red blood cells some of which could be observed enmeshed in the epithelial clumps. Cultures were negative.

The function of the right kidney was excellent. A pyelogram upon the left side revealed definite distortion of the pelvic outline with a "filling defect" in the region of the superior major calyx.

With a diagnosis of hypernephroma, a left nephrectomy was performed on September 30. The kidney was of normal size and its removal was not difficult. On its posterior surface, just below the level of the hilus, there was a small, rounded protuberance of obviously in-

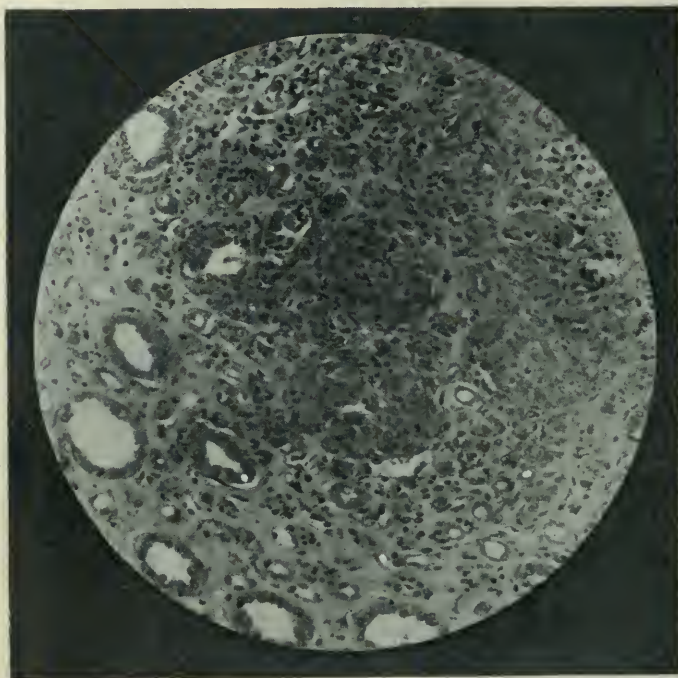


FIG. 2. FROM CASE I

High power photomicrograph which shows extension of the papillary carcinoma of the pelvis into pyramid of kidney; as represented by solid epithelial masses in the center of the field.

creased vascularity. Immediate section of the organ found it to contain two separate and distinct types of tumor. What was apparently a hypernephroma had produced the nodule above described, while the upper portion of the renal pelvis was filled with papilloma.

The convalescence was entirely uneventful, and the patient was discharged from the hospital in good condition on the fourteenth postoperative day.

Pathological report. Material: Left kidney.

Gross description: The specimen consists of a left kidney which has been opened by a median incision. About 5 cm. of ureter is attached and there is considerable pelvic fat. It measures 12 by 4.5 by 5.5 cm. The capsule is stripped. The anterior surface shows no gross abnormality; faint depressions mark out the six original lobules. On the posterior surface, the capsule is slightly adherent to the upper quadrant,

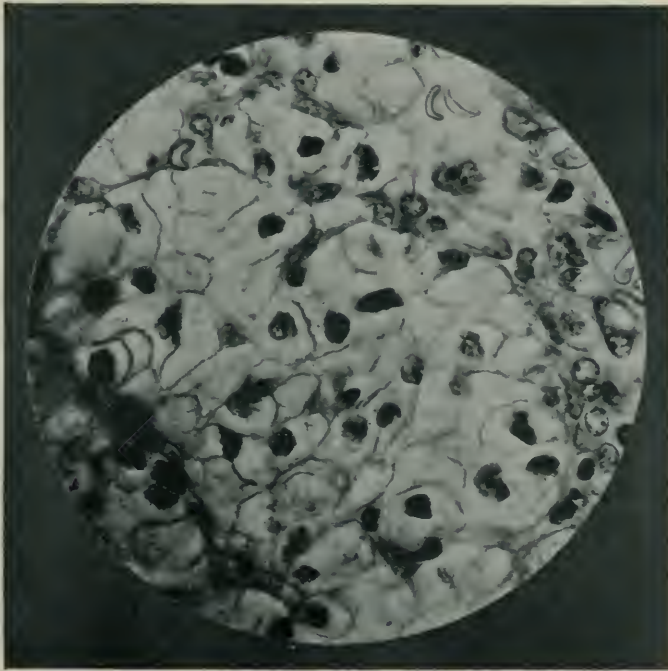


FIG. 3. FROM CASE I

Oil immersion objective, photomicrograph of hypernephroma

while the cortex is speckled with bright red, slightly projecting nodules giving a very coarsely granular appearance to this more or less well defined lobe. About 2 cm. from the hilum, on the posterior surface, a cyst 1 cm. in width projects above the level of the capsule. It contains a thin brown fluid. It suggests the ordinary retention cyst. Projecting from the lower pole and abutting on the hilum is a tumor mass 4 by 3.7 by 1.3 cm. It is firm, with an irregular, somewhat lobulated

surface. It is pale yellow in color, but there are numerous bright red petechial hemorrhages beneath its capsule.

The kidney viewed from within shows a relatively normal appearing cortex which averages 8 mm. in thickness. Glomeruli are of about normal prominence except in the upper pole. This portion shows thinning out of medulla and cortex, due to the presence of a cauliflower, fungating tumor mass arising, apparently, from the pelvis and filling its upper half. The tumor is grayish white, and intermingled with small blood clots. It consists of many papillomatous growths with common origin from a rather large pedicle and extending toward the cortex away from the hilum. Some of these outgrowths are long, narrow and quite villous in appearance. In the calices in the anterior wall there is a carpeting of pale, papillomatous tumor tissue which extends almost to the pyramids. The growth does not appear to invade the kidney proper and it stops short of the ureteral orifice. The lower half of the pelvis shows much injection of the mucosa and large, blotchy hemorrhages are quite conspicuous.

The tumor mass seen on the posterior surface has encroached upon the pelvis considerably. It is firm and well encapsulated. It is uniformly orange-yellow, and contains many small blood vessels. It extends from the level of the pelvis above, to 2 cm. from the capsule of the kidney below. It does not communicate with the pelvis in any portion. There is slight flattening of the pyramids below this tumor mass.

A frozen section of the cauliflower growth in the upper portion of the pelvis shows papillary carcinoma arising from the pelvic epithelium. The tumor in the lower pole is a hypernephroma.

Microscopic report. Eight sections are studied. Those cut perpendicularly through the cauliflower growth show a papillary neoplasm, arising from the pelvic epithelium. The growth consists of branching stalks of stratified squamous epithelium, similar to that of normal pelvic mucosa and supported by a loose-textured, vascular connective tissue. Numerous mitotic figures are present. In one of the sections, small groups of tumor cells have invaded the medullary portion of the kidney and are surrounded by numerous mononuclear cells and dense fibrous tissue. This growth is quite similar to a malignant papilloma of the bladder.

The remainder of the parenchyma shows patchy and diffuse scarring throughout the interstitial portion; pressure atrophy of some of the tubules; sclerosis of a few of the glomeruli and focal collections of mono-

nuclear cells. The smaller blood vessels are thickened while the larger ones present intimal sclerosis.

Sections of the firm yellow tumor projecting from the lower pole of the kidney reveal a new growth, composed of vacuolated cells, arranged in broad sheets and separated by a very delicate connective tissue stroma, in which are numerous capillaries and larger endothelial-lined blood spaces. No lumen formation is discerned. There is variation in the individual cells, the majority having a sharply defined outline with a pale red, finely granular, vacuolated cytoplasm. Other cells have less clearly demarcated borders with closely packed, deeper red granules in the cytoplasm. No nuclei are seen in many of the large, vacuolated cells. In others the nuclei are round, and vesicular with a dark staining nucleolus. In still others, they are stained deeply blue.

This is a typical picture of the neoplasm regarded as hypernephroma.

Diagnosis: Papillary carcinoma of the pelvis with extension into the kidney. Hypernephroma. Chronic vascular nephritis.

Case 2. A Russian factory-worker, aged fifty-two years, entered the Peter Bent Brigham Hospital on September 24, 1920, complaining of hematuria.

The family and marital histories were unimportant. The past general health had been good. He had had measles in childhood, and typhus fever in early adult life. There had been no other serious illness.

Six weeks before his admission to the hospital, the patient noticed that his urine was red in color. A similar change was observed intermittently at frequent intervals thereafter. Each period of bleeding was of three to four days duration. Slight backache was also reported. This had been present before the onset of hematuria. There were no other symptoms save for nocturia which had occurred once each night for many years. The general health was unimpaired; there had been no loss of weight.

Physical examination found a well developed and well nourished adult male of middle years, whose appearance was not suggestive of critical illness. The general examination was essentially negative. The temperature, pulse, and respirations were normal. The urine was yellow, cloudy, alkaline; specific gravity: 1.020. A slight trace of albumin was present in one of four examinations; sugar was absent. Microscopy: A few red blood corpuscles were reported in one of four examinations. White blood cells and casts were not found. Excretion of phenolsulphonephthalein, in two hours: 70 per cent. Hemoglobin: 90 per cent. White blood count: 8600. Blood pressure 150/90.

Cystoscopic examination found the bladder picture to be normal. The ureteral orifices were normal in position and appearance. The left ureter was readily catheterized and clear urine, which was microscopically negative, was obtained from the left kidney. Along the right ureter, a no. 5 catheter was passed for the full distance with definite difficulty. No flow of urine was obtained.



FIG. 4. FROM CASE II

Low power photomicrograph showing papilloma of the renal pelvis

Routine X-ray studies of the urinary tract were negative. In the making of a pyelogram, however, 19 cc. of sodium bromide solution were injected into the pelvis of the right kidney. A definite dilatation was demonstrated, but the pyelogram shadow was unusually faint and ill defined.

With a diagnosis of hydronephrosis of unexplained origin, operation was performed on October 6. The right kidney was found to be large, tense, and adherent. The pelvis and upper ureter were firmer than

normal in consistency, and definitely dilated. A pyelotomy wound permitted the escape of urine which was apparently stained with old blood, and through the defect in the pelvis there bulged soft, friable tissue which was unmistakably of tumor origin. Well below the level of dilatation and thickening, the ureter was divided and a nephrectomy performed. Immediate section of the kidney revealed the presence of

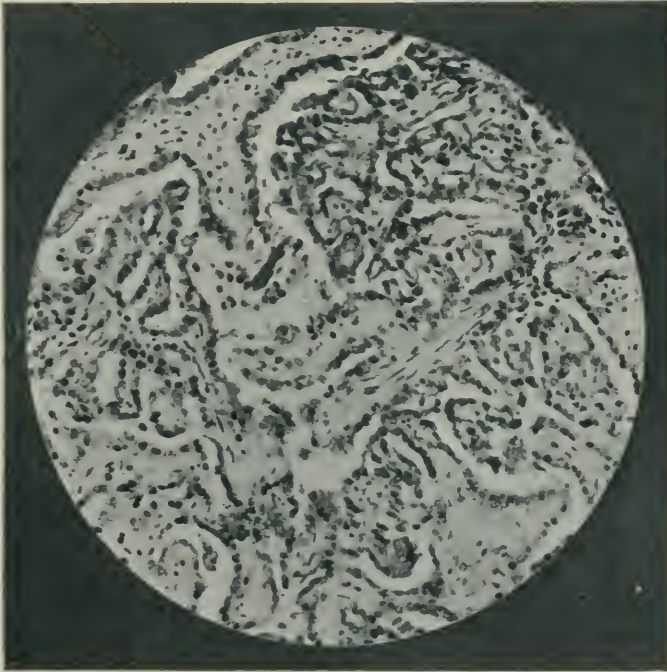


FIG. 5. FROM CASE II

High power photomicrograph which shows the papillary cyst-adenoma in the cortex of the kidney.

a large, villous tumor which completely filled a very much distended pelvis and encroached upon the lumen of the upper ureter. In the region of the lower pole of the kidney beneath the capsule, was found a small circumscribed nodule, pale gray in color.

The convalescence was satisfactory, and the patient was discharged to his home in good condition on the thirteenth postoperative day.

Pathological report. Material: Right kidney.

Gross description: The specimen consists of a right kidney which has been opened by median incision. The capsule strips easily. The surface of the organ is not remarkable except for several pale projecting cysts, the largest 12 mm. in diameter. The pelvis is considerably dilated and 7 cm. of ureter is attached. The picture viewed from within is very striking.

The main feature is a massive, papillary, fungating growth occupying the greater part of the pelvis, closely following the epithelial lining of the calices and extending 3 cm. into the ureter, which it practically occludes. The main tumor is white with the tips of many of the papillary growths quite vascular and red. Many of the calices contain dark red blood clots. At the upper pole the growth is less prominent but hemorrhages are observed beneath the mucosa and considerable thinning of the cortex has occurred. The lower part of the pelvis is occupied by the major portion of the tumor, the mass projecting nearly 2 cm. into the pelvic chamber. That lining the calices is more fungiform, forming a rather thick, gray, nodular layer which extends over the entire surface of many calices but does not entirely cover others. Implantations of more recent tumor growth are present in the calices of the upper pole and they vary in appearance from minute, slightly raised plaques to irregular nodular projections 4 to 5 mm. in height.

The cortex of the kidney shows considerable irregularity; glomeruli do not stand out prominently and arteries appear thickened. Cortex and medulla are pale, studded with bright red, petechial hemorrhagic areas, and there appears to be considerable invasion by connective tissue.

In the lower pole covered externally by the renal capsule, is a grayish white tumor growth, rather oval in shape, projecting about 1 mm. above the surface and extending into the cortex about 4 mm. It does not appear encapsulated but is fairly well outlined and is definitely embedded in the substance of the cortex. There are numerous small blood vessels visible on the cut surface. The tumor is slightly spongy in consistency.

Microscopic report. A section of the pelvic tumor shows wide, papillomatous outgrowths of stratified pelvic epithelium. These are closely packed and form blunt villous projections into the pelvis. These villi are supported by a central cord of connective tissue in which run a few thin-walled blood vessels. Groups of dilated capillaries, some of which have ruptured on the surface, are found at the tips of some of the villi. The growth does not extend into the edematous kidney paren-

chyma. Below the basal layer, however, are seen numerous small foci of mononuclear cells.

The oval white tumor located in the lower pole beneath the capsule consists of spaces lined by cuboidal epithelium. It has a complex arrangement resolving itself into relatively small cysts filled with papillary branching projections. The connective tissue stroma is relatively prominent and is abundantly supplied with capillaries.

Diagnosis. Papilloma of renal pelvis. Papillary cyst-adenoma of kidney.

In each of these cases the presence of combined tumors was evident upon examination of the gross specimen. It will be noted that in the kidney of case 1, there existed two separate and distinct epithelial tumors, both of which were malignant. In case 2, both growths were epithelial and apparently benign. (As has been pointed out in the thesis of Mock, however, the benign character of a papilloma can hardly be assured without a study of the entire mass in serial sections.) The association, in each instance, of a pelvis tumor with one of the renal parenchyma, is unusual, and so far as we have been able to determine, similar cases have not been recorded. There were no sarcomatous elements, and in neither case could there be any question of developmental relationship between the combined growths.

Obviously, the foregoing record is noteworthy not only because of the presence of two distinct types of neoplasm within the same kidney, but also because the pelvic papillomata in themselves are uncommon. Mock, in his excellent Paris thesis on "*Tumeurs Primitives du Bassinet*," found but ninety-four epithelial tumors of the renal pelvis, sixty-four of which were papillomatous. Hryntschak, in a recent paper "*Ueber Nierenbeckenpapillome*," reported a papillary pelvic growth and gathered from the literature sixty-seven additional case records. Rolando has very recently recorded still another instance of a tumor of this type.

In our own literature relatively few pelvic papillomata have been described. Reynolds, in 1904, reported one case, and Boucher one in 1905. McCown, writing in 1920, reviewed ten other American cases, one of which he himself presented. In

the discussion which followed his paper, Braasch, Kretschmer, and Goldstein mentioned six additional instances in which this type of tumor had been found. Sherwood and Herrick, in 1919, and Stevens, in 1920, reported single cases. Very recently three papillary pelvic growths have been described by Colston, by McGlannan, and by Miller and Herbst. Case 1 and case 2, presented in this paper, are the first cases of renal pelvis papillomata to appear in the records of the Peter Bent Brigham Hospital.

The hypernephroma and the simple renal adenoma are sufficiently common to need no extended discussion in this paper.

Apart from their rarity, these cases have been of interest from a diagnostic point of view. Obviously in each instance the tumor of the pelvis produced the clinical picture. In harmony with the sex predominance and age incidence observed by most of those who have written concerning renal pelvis papillomata, both patients were male and both were fifty-two years old. In one the right side was involved; in the other the left. In neither case was there any past record of importance. In both, as is so very frequently the case, total hematuria was given as the initial symptom and the chief complaint. (Mock found bleeding to be the first sign of disease in 41 per cent of his cases.) In case 1 the symptoms were of one year's duration. In case 2 the hematuria had begun but six weeks before admission to the hospital. The bleeding was intermittent in both instances. Neither patient reported symptoms of bladder irritability. Case 1, however, had noticed the occurrence of dull lumbar pain preceding his periods of hematuria. This may undoubtedly be ascribed to intermittent hemato-nephrosis to which Israel gives so great significance in the diagnosis of renal pelvis tumors. But one of the two patients complained of loss of weight and strength.

In neither case did the routine physical examination reveal the presence of a tumor, although it seems that in case 2, at least, a mass should have been palpated. The urine in case 1 contained many white blood cells, and a few red blood cells, while in case 2 only rare red blood corpuscles were found. A slight blood-stained flow was obtained from the affected side in case 1; no urine could be collected in case 2. It is important to note that

in the former instance, the product of the side of the lesion revealed upon microscopy clumps of degenerated epithelial cells. Such a finding is of extreme diagnostic importance, especially in the absence of chronic pelvic infection.

Pyelography served as the court of last appeal in both instances. In one a "filling defect" was shown; in the other a hydronephrotic dilatation, the shadow of which was faint and ill-defined.

It is interesting that in the first case the bleeding papilloma served as a warning without which the hypernephroma must almost surely have advanced to the stage of hopeless metastases. With regard to stones and chronic infection as possible etiological factors in the development of renal pelvis tumors, it is important to note that neither calculi nor evidences of chronic pyelitis were present in these cases. (Mock found stones reported in 14.5 per cent of his cases of pelvic neoplasm.²)

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² We are indebted to Dr. S. B. Wolbach for the preparation of the photomicrographs.

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PLATE I

Case I. Posterior view of the left kidney, showing at the upper pole, cortical irregularities due to the tumor in the pelvis; and at the lower pole, the hypernephroma.



PLATE II

Case I. Papillary carcinoma of renal pelvis (upper pole) and hypernephroma (lower pole).



PLATE III

Case II. Posterior view of right kidney, showing the pelvis and upper ureter greatly distended by tumor.



PLATE IV

Case II. Papilloma of renal pelvis, and papillary cystdenoma of kidney (lower pole).



TROPICAL INGUINAL GRANULOMA IN THE EASTERN UNITED STATES¹

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We wish in a preliminary report to briefly call your attention to a condition supposedly occurring only in the tropics, and its endemic existence in the temperate parts of the eastern United States.

Under the following variety of names: tropical inguinal granuloma, tropical ulcer, venereal granuloma, granuloma inguinale, and granuloma pudendi, there has long been recognized by physicians practising in the tropics and especially in South America a disease which was supposedly limited to these countries.

Last year Symmers and Frost reported from the laboratories of the Bellevue Hospital, New York, two cases of tropical inguinal granuloma found in negroes of that city, and this number has recently been augmented in a later report by Campbell of three further cases found in the urological wards of that institution.

Recognizing the similarity of the lesions, as illustrated by Symmers and Frost, to certain cases that have been repeatedly seen on the urological service of the Philadelphia General Hospital, a round-up was instituted on commencing the service January 1 with the result that 5 men and 2 women were found, in the institution suffering from this condition. These numbers have been increased since that time by 3 men and one woman patient, making a total of 11 cases under observation. Four further cases have been reported to us: one an inmate of the Penitentiary who had on two previous occasions been treated

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for this condition at the Philadelphia General Hospital; a second and a third, observed by Dr. A. H. Lippincott of Camden, New Jersey, after being diagnosed by our laboratory; and a fourth, a native of New Jersey who is awaiting hospital admission having been referred by Dr. J. L. Herman: a total of 15 cases.

The first and most important fact, when making such a diagnosis of a supposedly tropical disease as present in the temperate zone, is the unquestioned accuracy of the diagnosis. We have turned to the work of Aragao and Vianna of Rio Janeiro, who are probably the world's authorities on this condition, and the originators of the specific antimony treatment, and we have been able to corroborate and substantiate in our cases all the bacteriological data that they report, while the result of the specific treatment, and the similarity of the appearance of the lesions, as we have seen them, to the splendid photographic and colored illustrations in their work have alone been almost self-substantiating.

This disease has been present, practically constantly, in the Philadelphia General Hospital as long as any of the attending physicians and nurses can remember. It has masqueraded both here as elsewhere, under various other diagnoses, among which may be mentioned lues, now ruled out as in fact it has always been, by the repeatedly negative blood tests, lack of specific history and absolutely negative results with arsenic therapy; as chancroidal infection, to which it rarely bears any similarity as destructive ulceration is particularly not a characteristic; as tuberculosis, though never substantiated by microscopic study; as condylomata, to which when seen in the female or about the anal region it bears a close similarity; and as carcinoma, to which the microscopic picture in two of our cases was almost typical.

HISTOLOGICAL RECORD OF INGUINAL GRANULOMA²

Four cases: 2, 11, 6, 7. Tissues were fixed twenty-four hours in formalin; sections were cut from paraffin blocks and stained with hematoxylin and eosin.

² By Dr. William P. Belk.

The general appearance of the four was the same. There was a proliferation of fibrous tissue, moderate in amount, and enormous numbers of polymorphonuclear leucocytes and endothelial cells. Some times one, sometimes the other predominated. The vessel walls were somewhat thickened, as in chronic inflammatory processes. There was in every case some proliferation of the squamous epithelial cells of the skin; in no. 7 this was quite marked, and in no. 6 proliferation was so marked and extended so deeply that a preliminary diagnosis of epithelioma was made. There was in some cases, slight amount of necrosis, but this was never marked, nor was abscess formation noted. The process was separated from normal tissue by bands of connective tissue.

Sections from two rabbits autopsied. Rabbit 3 and rabbit 5 showed identical histological pictures. In these cases, the infecting organism was stained in the tissues by the following method: six hours fixation in Sheuder's solution, 1 hour in Giemsa stain, otherwise technique as ordinarily recommended for Giemsa.

BACTERIOLOGICAL METHODS AND LABORATORY DIAGNOSIS³

Direct smears

Direct smears from the lesions, properly prepared and stained, constitute a very reliable method of diagnosis. The material may be collected on sterile cotton applicators for either the smears or the cultures. Thin spreads of this material are essential. These are dried quickly in air and stained either by Wright's, or Geimsa's stain. Wright's method is the more rapid and has given satisfactory results. The most difficult part of the procedure is to obtain the proper differentiation of the stained smear in distilled water. Even with the most intense Wright's staining this differentiation should not be carried on for more than fifteen or twenty seconds. Application of the water for too long entirely decolorizes the capsules of the organisms: for too short a period, the capsules appear blue and the morphology of the bodies of the organisms cannot be observed clearly. With the best staining results, the organisms appear as small rounded pink bodies with a dark blue coccoid body in the center; or, more frequently, as oval pink bodies with a bacillary, or diplococcoid body occupying the longitudinal axis. The pink outer zone is a wide bacillary capsule; the dark blue central bodies represent metachromatic granules within

³ By Dr. James C. Small.

the bacillary body proper. The true outline of the bacillary body can be seen only after the capsule has been entirely decolorized by differentiating with distilled water. In stained smears from the lesions, some areas show organisms with capsules stained pale blue and obscurely differentiated central bodies; other areas show well defined dark blue metachromatic granules surrounded by a pink capsule, which latter, however, obscures the outline of the bacillus proper; and still other areas are seen in which the capsules have been entirely unstained and where the organisms appear as short, thick bacilli with rounded blunt ends occupied by the dark blue metachromatic granules. The organisms thus present a true bipolar-stained appearance with the intervening body shaft of the bacillus stained a pale blue. Always a few bacilli, shorter than those just described, stain solidly a deep blue.

The organisms are found within the cytoplasm of large mononuclear cells. In such they have well defined capsules, or may appear as nests of bacteria occupying a rounded area within the cell and revealing no capsules. In such nests the bipolar staining may be observed. The polymorphonuclear leucocytes do not contain encapsulated forms. Encapsulated forms may appear free, or in relation to cellular detritus. In the latter instances they occur chiefly in groups and in the neighborhood of large naked mononuclears. These presumably represent organisms released from the disintegrated cytoplasm of mononuclear cells. In the former instances they may occur singly and in no relation to cellular detritus.

Smears from the lesions are remarkably sparse in bacteria, as compared with smear preparations from other types of ulcerative lesions about the genitalia. Staphylococci, streptococci, diphtheroid bacilli and bacilli having the morphology and staining character of the colon group have been observed widely scattered, or in small clumps within the polymorphonuclear cells.

Cultures

The granuloma organisms have been grown in cultures in four instances. Of the various media and methods tried, surface inoculation of Sabaraud's maltose agar (2 per cent acid), as recommended by Aragao and Vianna, proved the most useful. This degree of acidity tends to inhibit some of the contaminating bacteria, and permits profuse growth of the granuloma bacillus. The growth is quite characteristic after twenty-four hours incubation. Colonies appear slightly gray white,

moist, glistening, dome shaped on round regular basis from 1 to 3 mm. in diameter. When touched with an inoculating wire they appear quite viscid and have the consistence and appearance of thin starch paste. By transmitted light they are translucent and have a slight brownish tinge. They are usually the largest colony appearing in these mixed cultures of the material taken directly from the lesions, and are very readily recognized.

In subcultures growth occurs on all of the simpler media. Enriched media is not necessary, on semisolid media the character of the growths does not differ essentially from that described above. In fluid media there is diffuse turbidity with a surface ring tending to adhere to the sides of the culture tube and to climb slightly above the level of the liquid. Later sedimentation occurs. Growth is profuse even in 1 per cent peptone water. In litmus milk there is acid production and coagulation within twenty-four hours. On potato growth is profuse, moist and slightly brownish in color. There is a decided blackening of the potato.

Smears from cultures, when stained with Wright's stain, show essentially the morphologic details previously described; in smears from Sabaraud's media and from moist glucose or plain agar, wide capsules are readily demonstrated, so that the organisms appear as do the encapsulated ones in direct smears from the lesions. In smears from broth cultures, capsules are not demonstrated, so that the organisms from twenty-four hour old cultures appear as short, plump bacilli exhibiting irregular staining—for the most part showing a dark area at either pole with pale blue intervening. In older cultures, especially in media containing a carbohydrate which has been fermented with decided acid production, long forms occur. These forms also stain irregularly, presenting dark blue banded areas, alternating with pale blue areas throughout the length of the organism.

Our study of the organism may be tabulated briefly:

Non-motile, non-sporulent, encapsulated bacillus, Gram negative; showing metachromatic granules as well as capsules with Romanowski staining.

It does not liquefy gelatin, or coagulated serum.

It hemolyzes blood in agar plates.

It does not form indol.

Coagulates and acidifies milk within twenty-four hours.

It ferments dextrose, levulose, lactose, galactose, saccharose, malatose, arabinose, mannitol, salicin, inulin, and dextrin. It does not ferment dulcitol and rice starch.

Pathogenicity

Intraperitoneal inoculation kills white mice and guinea pigs in twenty-four to forty-eight hours. The organisms are recovered at autopsy from the peritoneal fluid, the blood and the various internal organs.

Cutaneous inoculations of white mice, guinea pigs, rabbits, cats and dogs all failed to produce definite lesions.

Intradermal inoculations of dogs were also negative.

Subcutaneous inoculation of white mice and guinea pigs produced an inflammatory reaction, going on to abscess formation in some instances but always with spontaneous and rapid healing. In dogs and cats no abscess formation occurred, only a slight inflammatory reaction being noted.

In rabbits it produced large subcutaneous infiltrations with abscess formation and spontaneous rupture producing ulcers some of which have failed to heal after an observation period of six weeks.

CLINICAL STUDY

Symptoms

The usual history is that the lesion started as a small papule, non-inflammatory, which after rupture and the exudation of a slightly purulent fluid, refused to heal, and exhibited progressive tendencies toward slow proliferation and spreading. The lesion in its purity (especially seen when involving the inguinal region), is a flesh-red, exuberant, overgrowth of soft granulation tissue. It has absolutely no similarity to an ulcer, with its eroding, undermining, necrotic base. The center of the granuloma appears slightly depressed, and there is certainly a destructive action present, but the edges are redundant and overlap the apparently healthy skin margin. Exudate is scant, mucoid in character, of a non-offensive odor, and when wiped with gauze is easily removed, leaving a clean blood-red surface, similar in every respect to a large area of healthy granulation tissue as seen in clean surgical wounds. This picture varies according to the duration, size and location. The older lesions show at times tendencies towards cicatrization at some points, while spreading in others, but this only occurs when flat non-

chafing surfaces are involved. Large lesions, especially those in the perineum, become bulbous, simulating condylomata acuminata, with large rounded heads of new growth, the heads oftentimes with pearly white surfaces of epithelization, and deep crypts with raw granulomatous surfaces. Secondary infection here causes the clean, odorless character to change.

As indicated by the name the most frequent location is in the groin spreading upward as far as the anterior superior spine and downward through the fold of the groin frequently involving the perineum, and in some cases following the fold of the nates and spreading to the buttocks. Prepuccial lesions are likewise frequently associated and at times primary, and involvement here has given us the most destructive picture with a gradual erosion of the glans and even the shaft of the organ. In the female, the labia majora share the brunt of the attack with the perineum and groin involvement in some cases. We have had one case, a male, with the granuloma limited to a proliferative growth about the anus.

The patient has few subjective symptoms. They suffer no pain or discomfort unless the involved areas are so placed as to cause chafing. The granuloma is practically painless to the touch, and only deep pinching-up of the mass will cause suffering. Practically all of our patients have shown a definite degree of secondary anemia, but there has been a complete absence of pyrexia, chill, leucocytosis, throbbing, lassitude, or the usual concomitants of infectious processes.

Race

All of our cases, with one exception, have occurred in the negro. The one exception is that of a white male, in whom the lesion has likewise been atypical, simulating a phagodenic chancroidal sore with ragged ulcerated edges. His bacteriological examination was positive and he may be harboring a double infection. He, however, has not responded to treatment as in the others.

Diagnosis

We have based our clinical diagnosis entirely on the bacteriologic finding of the specific organism. This is done by making smears from the exuding surface, in which will be found numerous large mononuclear plasma cells, whose protoplasm, on proper staining, will be found studded with the characteristic encapsulated diplo-bacillus. The therapeutic result from the use of antimony intravenously, may likewise be taken as indicative of the accuracy of the diagnosis, for after three or four administrations the organism disappears entirely from the surface and cannot be found in smears.

Treatment

As pointed out by all previous writers and substantiated by the histories of cases in the Philadelphia General Hospital in years gone by, the treatment of these lesions has been most disappointing until the present, when antimony was first instituted.

Local applications of salves, escharotics, and antiseptics do no good whatsoever; vaccine therapy has been consistently a failure; excision is followed almost uniformly by recurrence before healing; arsenic is of no benefit; and X-ray alone has given us any curative results, causing a slow cicatrization, but because of the dangers associated with its use, it has been possible to apply it only once every three weeks, and therefore requiring on an average from twelve to eighteen months to establish healing. Even with X-ray the hospital experience in the years past has been disappointing, and probably at least 50 per cent of the cases had recurrences.

Some of our present cases have had two or more admissions in passing years for return of their lesions after apparent complete healing under X-ray therapy, while several have been so long inmates of the institution that they have been put on the hospital's pay-roll and work as laborers about the buildings.

Following Vianna's work, we started giving antimony intravenously in the form of tartar emetic. The initial dose of 0.04 gram was used, and this quickly advanced to a maximum dosage of 0.1 gram. Our first treatments were given daily and most

patients tolerated this until about ten doses had been given, but nearly all after that amount showed some symptoms of intolerance for the drug and we began intermitting the daily dosage, governing the time by symptomatic data. This intolerance consisted of rheumatoid pains in the joints associated with stiffness, especially seen in the early morning on rising, and most frequently located through the shoulder girdle, and as a general rule wearing off during the course of the day. There have not been in any case symptoms of an alarming character.

The drug has been prepared by dissolving 0.1 gram in 10 cc. of saline solution and is best put up and preserved by sealing, under sterile precautions in that size glass ampoules. Intravenous administration is essential.

The lesion becomes bacteriologically sterile after the second or third dose of the tartar emetic. Healing commences within forty-eight hours after the first administration, and from then on almost daily progress can be appreciated. Epithelial proliferation starts at the edges and rapidly spreads inward, while often isolated islets of epithelium in the midst of the granuloma, before not seen, or buried, start proliferation in the midst of the lesion and hurry the complete healing.

The phenomena of healing can best be pictured to you by comparing it to the use of salvarsan in somewhat similar long standing and untreated luetic skin lesions.

In some cases the administration of the drug causes a tingling, pricking sensation in the granuloma, immediately after the injection, and oftentimes an excess of mucoid secretion occurs for the first few days. Scabbing over of the surface takes place wherever the raw surfaces are in apposition, and thin crusts form around the periphery of open areas.

Results

Of our 11 personally observed cases, 8 are healed. As this is but a preliminary report we will omit history resume and tabulate them in the following table. Following the advice of Vianna we have persisted in giving all patients a course of injections after complete healing has been accomplished to prevent the possibility of recurrence.

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